VOLUME 33 JUNE 1940 NUMBER 6

Southern Medical Journal

Journal of the Southern Medical Association

Copyright, Southern Medical Association, 1940. Published monthly by the Southern Medical Association, Empire Building, Birmingham, Alabama. Annual subscription, $4.00. Entered as Second-Class Matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, November 12-15, 1940

TABLE OF CONTENTS

Carcinoma of the Lung: An Analysis of 195 Cases with a Special Note on Needle Puncture Biopsy. C. J. Tripoli, New Orleans, Louisiana, and Lang F. Holland, Austin, Texas 559

Discussed by George J. Taquino, New Orleans, La.; T. K. Lewis, Birmingham, Ala.

The Importance of X-Ray Interpretation in the Treatment of Pulmonary Suppuration. Brian Blades, St. Louis, Missouri 565

Discussed by Vincent W. Archer, Charlottesville, Va.; Walter S. Lawrence, Memphis, Tenn.; W. W. Robinson, Memphis, Tenn.; Charles H. Heacock, Memphis, Tenn.

The Biologic Action of Radiant Energy. Eugene R. Whitmore, Washington, District of Columbia 572

Discussed by Wright Clarkson, Petersburg, Va.; George T. Caldwell, Dallas, Tex.

Stones of Recumbency. Hjalmar E. Carlson and Nelse F. Ockerblad, Kansas City, Missouri 582

Discussed by Linwood D. Keyser, Roanoke, Va.; Thomas D. Moore, Memphis, Tenn.; Jefferson C. Pennington, Nashville, Tenn.; Henry J. Lindner, New Orleans, La.; Jarratt P. Robertson, Birmingham, Ala.; Alexander Randall, Philadelphia, Pa.

The Grading of Rectal Cancer. Tom E. Smith, Dallas, Texas 593

Discussed by Mark M. Marks, Kansas City, Mo.; T. C. Moss, Memphis, Tenn.; Curtice Rosser, Dallas, Tex.; Marion C. Pruitt, Atlanta, Ga.

An Electrically Lighted Anoscope with Detachable Handle. J. H. Dodson, Mobile, Alabama 600

Measles Complicating Pregnancy: Report of Twenty-Four Cases with Three Instances of Congenital Measles. Isadore Dyer, Tahlequah, Oklahoma 601

Discussed by Robert A. Strong, New Orleans, La.

Cerebellar Abscess: Review of Cases. Harry Wilkins, Oklahoma City, Oklahoma 605

Discussed by Joseph E. J. King, New York, N. Y.; Nicholas Gotten, Memphis, Tenn.; Dean H. Echols, New Orleans, La.; Hermon S. Major, Kansas City, Mo.

The Etiology of Nerve Deafness with Particular Reference to Quinine. S. B. Forbes, Tampa, Florida 613

Discussed by John H. Foster, Houston, Tex.; Charles D. Blassingame, Memphis, Tenn.; Albert L. Bass, Louisville, Ky.; Murdock S. Equen, Atlanta, Ga.; C. C. Cody, Houston, Tex.

Primary Cutaneous Gilchrist's Disease. J. Lamar Callaway and Vince Moseley, Durham, North Carolina 622

Discussed by Everett C. Fox, Dallas, Tex.; M. T. Van Studdiford, New Orleans, La.; Harry M. Robinson, Baltimore, Md.

Studies in Obstetric Analgesia. Donald M. Paton, Houston, Texas 626

Discussed by M. J. Serwer, Oklahoma City, Okla.; Mary Catherine Baldwin, Riverside, Calif.

Serodiagnostic Tests for Syphilis as Performed in State Laboratories in 1938 and 1939: A Report of the Committee on Evaluation of Serodi-

Continued on Next Page

TABLE OF CONTENTS—Continued

agnostic Tests for Syphilis. H. H. Hazen, Washington, D. C.; Thomas Parran, Washington, D. C.; J. F. Mahoney, Washington, D. C.; Arthur H. Sanford, Rochester, Minnesota; F. E. Senear, Chicago, Illinois; Walter M. Simpson, Dayton, Ohio; and R. A. Vonderlehr, Washington, D. C. 633

Discussed by Arthur G. Schoch, Dallas, Tex.; R. A. Vonderlehr, Washington, D. C.

An Analysis of Periodic Physical Examinations for Five Years. J. J. Brandabur, Huntington, West Virginia 638

Discussed by W. J. Lancaster, Wilmington, N. C.; George A. Traylor, Augusta, Ga.

The Treatment of Typhoid Fever by the Thiazole Derivatives of Sulfanilamide: A Preliminary Report of Four Cases. J. O. Weilbaecher, Jr., Emma S. Moss, Henry M. Taylor, and Homer Dupuy, New Orleans, Louisiana 645

Some Medicolegal Aspects of Alcoholic Intoxication. Ferdinand C. Helwig, Kansas City, Missouri 648

Discussed by Owen S. Gibbs, Memphis, Tenn.; Wiley D. Forbus, Durham, N. C.; J. A. McIntosh, Memphis, Tenn.

Indications for and Results of Splenectomy. H. Dale Collins, Oklahoma City, Oklahoma 656

Discussed by Giles A. Coors, Memphis, Tenn.

The Roentgenologic Bone Manifestations in Certain Generalized Diseases of Infants and Children. W. D. Anderson and James G. Hughes, Memphis, Tennessee 660

A Note on the Effect of Alpha-Tocopherol (Vitamin E) in Human Nutrition. Tom D. Spies, Birmingham, Alabama, and Richard W. Vilter, Cincinnati, Ohio 663

EDITORIALS 665

The Louisville Meeting—Hobby and Art Exhibit
Potassium and Temperature
Laryngeal Papillomata and Estrogens
An Unscientific Movie
Twenty-Five Years Ago

BOOK REVIEWS 667

OFFICERS, Southern Medical Association and Organizations Meeting Conjointly 670

SOUTHERN MEDICAL NEWS 672

WILDER'S "CLINICAL DIABETES MELLITUS and HYPERINSULINISM"

By RUSSELL M. WILDER, M.D., Professor and Chief of Department of Medicine, The Mayo Foundation, Rochester, Minnesota. 475 pages, illustrated. Probable price $6.00.

Emphasis throughout on clinical consideration.

Protamine Zinc Insulin given extensive consideration.

Details provided for planning satisfactory diets to prevent malnutrition and overweight.

All the complications of diabetes—acute and chronic disturbances given full attention.

Detailed directions for treatment of acidosis.

Chapter on Hemochromatosis represented by more cases than have ever been reported from any one hospital or clinic.

Send Orders to

J. A. MAJORS COMPANY

New Orleans **Dallas**

Brimful of the NEW *Operative Technics You Want to Know—And Need to Know*

NEW FIFTH EDITION JUST OFF THE PRESS

HORSLEY-BIGGER

"OPERATIVE SURGERY"

New Features of 5th Edition

Among the new procedures included are ligation of the patent ductus arteriosus, segmental pneumonectomy, and extra-pleural pneumothorax.

There is a new chapter on PERITONITIS and the description of the treatment of APPENDICITIS has been considerably elaborated. Clute's incision is given for exposing the diaphragm, the terminal esophagus and the cardiac end of the stomach. The recent modification of Whipple's operation for excision of the duodenum and head of the pancreas and also the new operation of Brunschwig for this purpose are given.

Dodson's modification of Coffey's operation for transplantation of the ureters has been added.

The new technic for nailing intracapsular fractures of the hip, a bone peg for ununited fractures of the carpal scaphoid, Schanz's osteotomy, a new operation for hammer-toe and many other procedures are described.

By J. SHELTON HORSLEY, M.D., LL.D., F.A.C.S., and ISAAC A. BIGGER, M.D., with contributions by C. C. Coleman, Austin I. Dodson, John S. Horsley, Jr., and Donald M. Faulkner. Two volumes. Fifth Edition. 1521 Pages, 1442 illustrations.

PRICE, $18.00

Revised and Enlarged

The Fifth Edition of this popular set has been thoroughly revised, enlarged, and brought up to date with 171 pages of entirely NEW TEXT MATERIAL, and 183 NEW ILLUSTRATIONS describing and illustrating the NEWEST in operative procedures. These new methods have been proved to be sound by actual use in the operating room, as have all the procedures which this book presents.

Operations are described in narrative form, approximating the smooth regularity of actual operations in progress. The clearly detailed illustrations portray surgical technic in step-by-step fashion.

Particular stress is laid upon the preservation of physiologic function and the interpretation of the biologic processes that follow surgical operations. The authors emphasize the fact that because the object of an operation is to save life, to relieve pain, and to restore function, the technic of an operation should be chosen not solely because it appeals to a mechanical sense, but because it is biologically correct.

Use Coupon to Send for Your Set TODAY

The C. V. MOSBY COMPANY,
3525 Pine Blvd., St. Louis, Mo. SMJ 6-40

Gentlemen: Send me the new Fifth Edition of Horsley-Bigger "OPERATIVE SURGERY," priced at $18.00.

Dr._____

Address_____

First VITAMIN PRODUCT FOR MEDICAL USE MADE IN AMERICA

In 1919[1] Drs. T. B. Osborne, A. J. Wakeman and Lafayette B. Mendel announced a method of preparing vitamin B-complex. They visualized a vast clinical use for vitamins in concentrated form and the Harris Laboratories, Inc., were founded in 1919 to make such concentrate available for medical use. No other water-soluble vitamin has been so widely used and proven clinically as Yeast Vitamine (Harris) Tablets.

Yeast and Its Concentrate Should Not Be Evaluated Wholly by the Units of B_1 and B_2

This was an earlier conception, but has been disproven clinically.

PELLAGRA – Goldberger,[2] Spies[3] and others cured pellagra with large doses of Brewers' Yeast (Harris) before nicotinic acid was discovered. Clinical work with the isolated nicotinic acid (crystalline) has proven the effect of this substance (in the yeast)—years before discovery of its presence.

HERPES—Gerstenberger[4] reported cures of herpes lesions of mouth and tongue with Yeast Vitamine (Harris) Tablets before B_2 and nicotinic acid were isolated in the pure form. B-complex in the yeast performed this double duty.

Bottles of 50, 500, 1000.

B_4 and B_6 – These new vitamins now are appearing in the clinical picture. What effect are they producing?

They are all in Brewers' Yeast (Harris) with Yeast cell salts—nucleic acid and the lipoids

These groups doubtless have some therapeutic values, yet unrecognized.

Be Sure—Use "B-complex" as advised by Williams and Spies,[5] who state:

Even when vitamins B_1, B_2, B_6 and nicotinic acid are all combined, "it cannot fulfill the entire function of the vitamin B-complex."

•

Crystalline Vitamins B_1-B_2-B_6-C and nicotinic acid are offered in tablets of convenient sizes.

1 Jr. Biol. Chem., Dec., 1919
2 Pub. Health Reports, Jan., 1925
3 Jr. A.M.A., March 13, 1937
4 Am. Jr. Dis. Children, Oct., 1923
5 "Vitamin B_1", 1938, p. 133

THE HARRIS LABORATORIES
TUCKAHOE NEW YORK
SINCE 1919
FOUNDERS of VITAMINS for MEDICAL USE

Clinically superior to ephedrine in the relief of hay fever symptoms—

PROPADRINE HYDROCHLORIDE

PROPADRINE HYDROCHLORIDE, in its application in the symptomatic relief of hay fever patients, is pharmacologically equal to ephedrine and *clinically superior* because of its comparative freedom from side-reactions. Its clinical superiority has been emphasized by independent investigators in these statements:

1. Propadrine Hydrochloride may be administered in therapeutic doses with relative freedom from nervousness, insomnia, tachycardia and palpitation.

2. While the relief obtained from a single dose is equal to that produced by ephedrine, the absence of nervousness and insomnia makes it possible to use propadrine at frequent regular intervals and obviates the necessity of combining with it a sedative. Used in this manner, the results are definitely better than can be obtained by the usual irregular use of ephedrine.

3. The use of propadrine every three or four hours gave more relief to patients suffering with urticaria and angioneurotic edema than any other medication these investigators found.

4. In children, Propadrine Hydrochloride is not likely to produce restlessness or walking or talking in their sleep.

PROPADRINE HYDROCHLORIDE (phenylpropanol-amine hydrochloride) is supplied in these convenient dosage forms:

CAPSULES: 3/8 grain—bottles of 25, 100 and 500; 3/4 grain—bottles of 25 and 100.

SOLUTION: 1% (isotonic)—1-ounce and pint bottles; 3%—1-ounce and pint bottles. (For topical application as a vasoconstrictor in reducing congestion of nasal mucous membranes.)

NASAL JELLY: in 3/4-ounce tubes containing 0.66% Propadrine Hydrochloride.

ELIXIR: Each fluidounce contains 2 grs. Propadrine Hydrochloride. In pints and gallons.

"FOR THE CONSERVATION OF LIFE"

Pharmaceuticals *Sharp & Dohme* Mulford Biologicals

PHILADELPHIA

"Middle of the Road"

CONSTIPATION *often means water deficiency in the stool (dehydration).* • DIARRHEA *usually means water excess (superhydration).* • NORMAL BOWEL FUNCTION *means a balance between these two extremes.*

MUCILOSE

by influencing "water-balance" helps to provide a normalizing "middle of the road" therapy in constipation.

Mucilose is a hemicellulose (vegetable gum) prepared by a special process from the Plantago loeflingii. It possesses an unusual ability to swell in the presence of liquid and form a mucilaginous mass which eases natural elimination.

MUCILOSE GRANULES—Pleasantly flavored. No mixing required. 4 oz. and 1 lb. packages.

MUCILOSE FLAKES—Mixes well with liquids. 4 oz. and 1 lb. packages.

FREDERICK STEARNS & COMPANY • DETROIT, MICHIGAN
NEW YORK · KANSAS CITY · SAN FRANCISCO · WINDSOR, ONTARIO · SYDNEY, AUSTRALIA

FREDERICK STEARNS & COMPANY
Detroit, Michigan Dept. SM-6
Please send me a supply of Mucilose for clinical test.

*Name*_____ *M. D.*

*Address*_____

*City*_____ *State*_____

Help the mother

supply the fetal demand for

CALCIUM

this pleasant, effective way

CALCIUM storage in the human fetus begins at about the fourth month and becomes very rapid toward the end of pregnancy. Unless the amount of calcium and phosphorus ingested by the mother is greater than the fetal demand, there is danger of a severe drain upon the maternal organism or of the fetus receiving an insufficient supply.

To offset the deleterious effects of a lack of calcium and to compensate for vagaries in the patient's choice of foods which may result in a low calcium intake, many physicians prescribe Dicalcium Phosphate Compound with Viosterol Squibb—a readily absorbed source of calcium and phosphorus, with sufficient Vitamin D to assist in their adequate utilization.

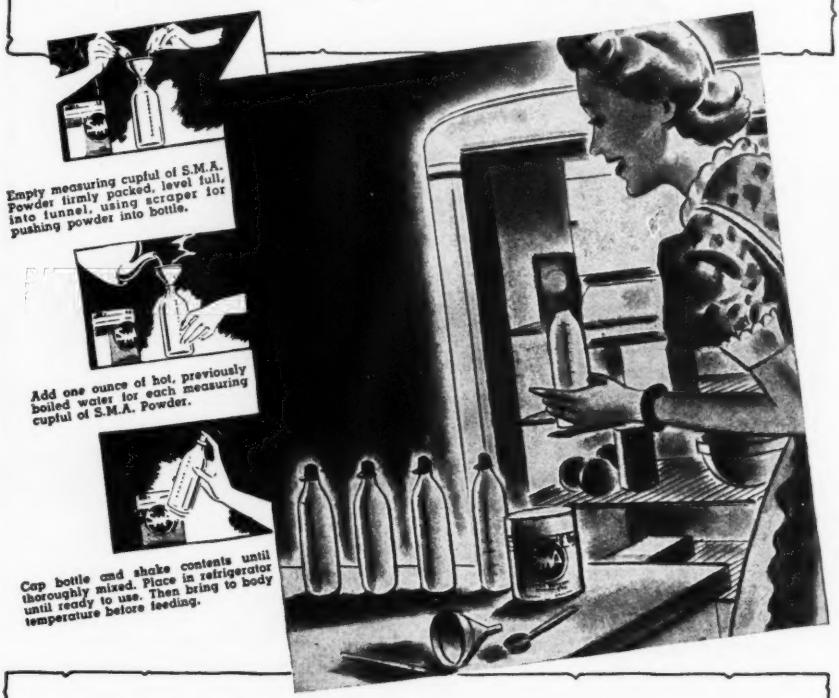
Dicalcium Phosphate Compound with Viosterol is available in both tablet and capsule form. The tablets are flavored with wintergreen and have a pleasant taste. Capsules are suggested as a change from the routine use of tablets, especially during pregnancy, which may require administration of a calcium preparation over a considerable period.

One tablet (or two capsules) contains 9 grains dicalcium phosphate, 6 grains calcium gluconate, and 660 U. S. P. XI units of Vitamin D. The usual dose for pregnant women is one or two tablets (2 or 4 capsules) three times daily. Tablets are available in boxes of 51 and 250; capsules in bottles of 100 and 1000.

For literature address the Professional Service Department
E. R. Squibb & Sons, 745 Fifth Avenue, New York, N. Y.

SQUIBB DICALCIUM PHOSPHATE COMPOUND *with* VIOSTEROL TABLETS CAPSULES

S.M.A. SAVES TIME—SAVES MONEY


Empty measuring cupful of S.M.A. Powder firmly packed, level full, into funnel, using scraper for pushing powder into bottle.
Add one ounce of hot, previously boiled water for each measuring cupful of S.M.A. Powder.
Cap bottle and shake contents until thoroughly mixed. Place in refrigerator until ready to use. Then bring to body temperature before feeding.

Enough For 24 Hours Made up at Beginning of Day

S.M.A. is so easy to prepare. Enough for the entire 24 hour period may be made up at the beginning of the day and stored in the refrigerator until ready to feed. It should then be brought to body temperature and fed at prescribed intervals.

S.M.A. is economical, too, because, aside from orange or tomato juice for the required vitamin C, no other vitamin supplements are usually necessary. S.M.A. provides vitamins A, B_1 and D in amounts sufficient for the normal, full-term infant. When kept in the refrigerator, it retains its nutritional value indefinitely.

S.M.A. IS ECONOMICAL. INFANTS RELISH IT, DIGEST IT EASILY AND THRIVE ON IT.

S. M. A. is a food for infants — derived from tuberculin-tested cow's milk, the fat of which is replaced by animal and vegetable fats including biologically tested cod liver oil; with the addition of milk sugar and potassium chlorides; altogether forming an antirachitic food. When diluted according to directions, it is essentially similar to human milk in percentages of protein, fat, carbohydrate and ash, in chemical constants of the fat and physical properties.

S.M.A. CORPORATION • 8100 McCORMICK BOULEVARD • CHICAGO, ILLINOIS

TO SUPPLEMENT INJECTIONS

GIVE MALE SEX HORMONE VIA PERCUTANEOUS ABSORPTION

Neo-Hombreol Dosules are sealed gelatin capsules, manufactured exclusively by us, containing an accurately measured quantity of Neo-Hombreol (testosterone propionate 'Roche-Organon') in a rapidly absorbable ointment base. Thus, for the first time is it possible in a practical way to administer this potent substance by inunction, free from the obvious danger of overdosage inherent in the use of bulk ointments packaged without measurement control of the individual dose. Each Neo-Hombreol Dosule contains 2 grams of ointment representing 4 milligrams of chemically pure synthetic testosterone propionate. Packages of 25.

NEO-HOMBREOL DOSULES

♂ Male climacteric, hypogonadism, and cryptorchidism; experimentally, in impotence and incipient prostatism.

♀ Premenstrual mastopathia, female climacteric, dysmenorrhea, and menorrhagia.

ROCHE-ORGANON, INC. • NUTLEY • N. J.
IN CANADA: ROCHE-ORGANON LTD. • MONTREAL • TORONTO

Constipation in Infancy

Constipation in infancy probably commands the physician's attention more often than any other symptom that points to the need of readjusting a feeding formula.

Constipation is a common complaint and oftentimes is the real reason for a slow gain in weight, restless nights and a fretful, uncomfortable baby.

Infants fed on milk and water in proportions suitable for healthy babies of given age and weight with an amount of Mellin's Food to meet the carbohydrate requirement (*six to eight level tablespoons to the full day's mixture*) are seldom constipated.

Many physicians use Mellin's Food routinely in preparing bottle feedings, for they know from experience that regular stools of good consistency are characteristic of babies fed on milk properly modified with Mellin's Food. These physicians thus avoid much of the trouble associated with infant feeding.

Mellin's Food Co., Boston, Mass.

MELLIN'S FOOD: Produced by an infusion of Wheat Flour, Wheat Bran and Malted Barley admixed with Potassium Bicarbonate—consisting essentially of Maltose, Dextrins, Proteins and Mineral Salts.

Laxatives

not needed to relieve

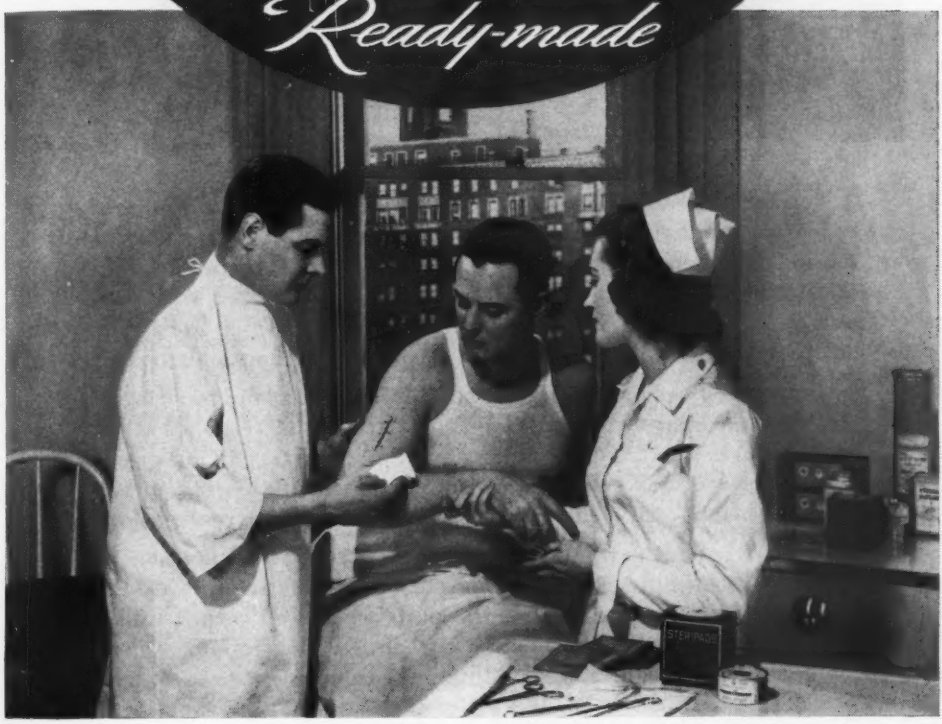
Constipation

when the daily feedings are prepared from milk properly modified with

Mellin's Food

Samples sent to physicians upon request.

STERILE DRESSINGS
Ready-made



● Steripads are ready-to-use, neat and uniform, for a host of minor dressings. They save time and eliminate cutting and folding gauze by hand. Steripads furnish protection without excessive bulk. They are packed in individual envelopes and sterilized.

Steripads are supplied in boxes of 25 or 100, sizes 3″ x 3″, openable to 3″ x 9″; 4″ x 4″, openable to 4″ x 16″.

ORDER FROM YOUR DEALER

COPYRIGHT 1940, JOHNSON & JOHNSON

STERIPADS

Johnson & Johnson

NEW BRUNSWICK, N. J. CHICAGO, ILL.

PAINFUL MENSES

may be relieved with

PROLUTON (INTRAMUSCULAR) · PRANONE (ORAL)

RELIEF is possible for many patients who suffer from dysmenorrhea and the distressing symptoms associated with premenstrual tension. Lackner, Krohn, and Soskin[1] report complete relief in 71.4% of a selected group of patients treated for dysmenorrhea with progesterone (*Proluton*). The authors point out that normal uterine development is essential for successful corpus luteum hormone therapy.

Premenstrual tension, with its accompanying disagreeable physical and nervous manifestations, responds to this treatment. Israel[2] states, "The administration of progesterone (crystalline corpus luteum principle) cured one and temporarily relieved six patients with premenstrual tension."

For the treatment of these cases, the physician now has a choice between intramuscular and oral medication. *Proluton* (progesterone), the pure crystalline corpus luteum hormone, is available for intramuscular injection. *Pranone* Tablets contain crystalline anhydro-hydroxy-progesterone. The progesterone-like effect of this substance when administered orally has been proved by Salmon, Walter, and Geist[3] who produced the characteristic changes in the endometria of post-menopausal women.

***Proluton* injections and *Pranone* Tablets are also indicated in functional Menorrhagia and Metrorrhagia, and in Threatened and Habitual Abortion.**

FOR ADDITIONAL INFORMATION, PLEASE ADDRESS THE MEDICAL RESEARCH DIVISION

1) Lackner, J. E.; Krohn L., and Soskin, S.: Am. J. Obst. & Gynec. 34: 248 (Aug.) 1937.

2) Israel, S. L.: J.A.M.A. 110: 1721 (May 21) 1938.

3) Salmon, J. J.; Walter, R. I., and Geist, S. H.: Proc. Soc. Exper. Biol. & Med. 40: 252 (Feb.) 1939.

SCHERING CORPORATION

BLOOMFIELD, NEW JERSEY

★ ★

Grapefruit and the Maternal Diet

NORMAL pregnancy and lactation greatly increase the demand for all of the food elements, because the fetus acts as a parasite. If its nutritional requirements are not met through the mother's diet, food materials are secured from her body, even to the extent of breaking down the maternal tissues. Calcium, for example, may be taken from her bones or teeth.

Of prime importance during this period is an abundant, well-balanced diet, one especially rich in calcium, vitamins, and mineral salts. The mother requires a generous intake of Vitamin C, both to maintain her own health and to ensure an adequate store to the infant at birth and a sufficient supply during lactation.

Citrus fruits are an outstanding source of Vitamin C, and they provide appreciable amounts of other vitamins as well as mineral salts, citrates, and easily assimilable sugars. *Moreover, the addition of citrus fruits to the diet increases the assimilation and retention of calcium derived from other foods.*

Many physicians, dentists and dietitians counsel the consumption of grapefruit juice *in addition* to the usual intake of citrus fruit. Its fresh and invigorating flavor makes it ideal. *Canned* grapefruit juice is high in all the values attributed to the fresh fruit, is convenient to use and readily available at all seasons.

Grapefruit may be taken at various times of day without affecting the appetite for the coming meal.

As a variant and supplement to the habitual consumption of citrus fruit, grapefruit juice helps to raise the usual "minimum" intake of vitamins and minerals to that "optimum" which makes for health in mother and child. In canned form, it is extremely economical.

The Citrus Commission of the State of Florida has prepared a treatise on the citrus fruits in their relation to health, with a full bibliography; a copy will be sent to any member of the medical profession upon request.

FLORIDA CITRUS COMMISSION
STATE OF FLORIDA

Florida Citrus Commission Dept. 28-M
Lakeland, Florida

Gentlemen:

Please send me your book, CITRUS FRUITS AND HEALTH.

Name_____

Address_____

City_____ State_____

Profession_____

The statements in this advertisement are based on the following numbered references in "Citrus Fruits and Health": 62, 63, 64, 65, 69.

Wyeth's

SULFUR FOAM APPLICATORS

for the External Application of Sulfur

WYETH'S Sulfur Foam Applicators eliminate the objectionable messiness, smell and discomfort of most sulfur ointments and are acceptable to the patient.

Sulfur Foam is an effective prophylaxis and treatment for scabies and is gaining popularity in other cases where sulfur is indicated externally.

In Sulfur Foam Applicators, the sulfur and a bland soap are impregnated in a special wash cloth. The patient merely moistens the cloth and lathers the area to be treated. The lather dries, leaving a film of sulfur in direct contact with the area.

Wyeth's Sulfur Foam Applicators are supplied in packages of three cloths.

YOU ARE INVITED TO WRITE FOR LITERATURE AND FREE SAMPLES

JOHN WYETH & BROTHER, INCORPORATED
PHILADELPHIA, PA. WALKERVILLE, ONT.

"...Casein Modified"

Made from fresh skim milk (casein modified) with added lactose, salts, milk fat, and vegetable and codliver oils.

In human milk 2/3 of the protein is in true solution, while in cow's milk only 1/6 of the protein is soluble. During the process employed in preparing Similac the soluble proteins in cow's milk are increased to a point approximating the soluble proteins in human milk. How greatly this improves the digestibility is indicated by a comparison of the curd (insoluble calcium paracaseinate) formed by cow's milk, with the soft flocculent curd of Similac. The softer the curd the shorter the digestive period.* Similac, like breast milk, has a consistently zero curd tension.

* Espe & Dye—"Effect of Curd Tension on the Digestibility of milk"—Amer. Journal Diseases of Children—1932, Vol. 43, p. 62.

SIMILAC } SIMILAR TO BREAST MILK

M&R DIETETIC LABORATORIES, INC. • COLUMBUS, OHIO

INFANTS IMPROVED

by diet addition of

KNOX GELATINE *(U.S.P.)*

A lower incidence of vomiting, diarrhea, and constipation resulted from adding 1% and 2% plain, unflavored gelatine to milk fed a group of infants two years ago. An additional advantage was a decrease in the incidence of upper-respiratory infections.

Repetition of this work* has substantiated the results.

PLAIN *(Sparkling)* KNOX GELATINE (U.S.P.) was used in all these studies.

CONVENIENT GELATINE PROPORTIONS:

1%

One envelope to 3 pints or 1 level teaspoon to 18 ounces of milk.

2%

One envelope to 1½ pints or 1 level teaspoon to 9 ounces of milk.

(Formula Sent Upon Request)

KNOX GELATINE

IS PURE GELATINE—NEUTRAL

NO SUGAR

SEND THIS COUPON FOR FREE REPRINTS

* Further Clinical Observations on Feeding Infants Whole Milk, Gelatinized Milk, and Acidified Milk, C. LORING JOSLIN, M.D., F.A.A.P.; Bulletin of the School of Medicine, University of Maryland; Jan. 1939.

KNOX GELATINE, Johnstown, New York, Dept. 408

Please send me above reprint.

*Name*_____

*Address*_____

Away from Home

★★ **Petrolagar**

Vacations mean a change of diet, water, exercise. Daily routine is altered and bowel Habit Time interrupted. This combination of circumstances tends to have a constipating effect.

Instead of quick acting harsh catharsis, the gentle softening action of Petrolagar promotes motility and encourages a regular, comfortably passed stool.

Petrolagar is miscible with liquids. It may be given orally or in an enema to assist in the restoration of a regular Habit Time of Bowel Movement.

Petrolagar . . . liquid petrolatum 65 cc. emulsified with 0.4 Gm. agar in a menstruum to make 100 cc.

Petrolagar Laboratories, Inc. • 8134 McCormick Boulevard • Chicago, Illinois

Hematinic Plastules

EXCEPTIONALLY WELL TOLERATED

● The effective daily dose of Hematinic Plastules is small—easily assimilated—*exceptionally well tolerated.*

Clinical tests prove a high incidence of tolerance, even in the anemias of pregnancy, where the gastro-intestinal tract is likely to be upset.

Indicated in cases of iron deficiency anemia, Hematinic Plastules are effective and economical.

℞ Hematinic Plastules Plain or
Hematinic Plastules with Liver Concentrate
Available in bottles of 50's and 100's

THE BOVININE COMPANY
8134 McCormick Boulevard • Chicago, Illinois

MODERN IRON THERAPY

When STASIS

threatens the biliary tract—

Ketochol provides reliable hydrocholeresis with maximum "flushing" action, increasing bile volume by an average of 144%*, thus acting as a physiologic cholecystotomy in relieving congestion.

A combination of the oxidized, or keto forms of those bile acids (cholic, desoxycholic, chenodesoxycholic, and lithocholic) normally found in human bile, Ketochol is widely used in the treatment of cholangeitis, chronic cholecystitis, biliary stasis due to hepatic dysfunction, and related conditions.

Average dose: one tablet t.i.d. with or immediately after meals.

Supplied in bottles of 100 and 500 tablets.

**Ivy, A. C. et al.: Amer. Jl. Dig. Dis., November, 1938*

G. D. Searle & Co.

Ethical Pharmaceuticals Since 1888

CHICAGO • New York • Kansas City • San Francisco

MUSCULAR RHEUMATISM

NEURALGIA

LUMBAGO

MYALGIA

FOR RELIEF OF LOCAL PAIN

PANALGESIC

APPLIED EXTERNALLY FOR LOCAL AND SYSTEMIC ANALGESIA

PANALGESIC, containing salicylates and camphoric terpenes in alcohol and a natural oil, acts as an effective **local analgesic, counterirritant** and **rubefacient** in various nerve and muscle aches and pains, such as Neuralgia, Myalgia, Lumbago and Muscular Rheumatism.

PANALGESIC enhances this local action by a systemic analgesic effect. Absorption of salicylates through the unbroken skin is favored by the alcohol content of Panalgesic. Ferric chloride added to the urine several hours after the topical application of Panalgesic will produce a violet color, as evidence of an appreciable absorption of salicylates.

PANALGESIC is a clear green liquid, rapidly absorbed through gentle massage. The skin is left relatively dry and free from oil or stain. The oil in Panalgesic prevents undue irritation of the skin—even when massage is vigorous.

PANALGESIC Contains

Camphoric Terpenes	(by weight)	4%
Salicylates	(by weight)	58%
Alcohol	(by volume)	22%
Natural Oil	(by weight)	20%

Issued in Two Ounce and Half Gallon bottles

Not advertised to the laity

WILLIAM S. Poythress & CO. INC. RICHMOND, VIRGINIA

Since 1856

Three servings per day of COCOMALT comprise an extremely valuable means of supplementing vitamins and minerals in both normal and therapeutic diets. The customary daily ration of three servings of COCOMALT contains:
Vitamin A 2400 I. U.
Vitamin B 225 I. U.
Vitamin G 150-225 S. B. U.
Vitamin D 402 I. U.
Calcium 450 mg.
Phosphorus 480 mg.
Iron 15 mg.
Cocomalt
TRADE MARK
MALTED FOOD DRINK

Cocomalt Alone

Gives High Nutritional Value

In almost every instance COCOMALT is served with milk . . . yet the nutritional value of milk may vary to such an extent through the seasons that an analysis of COCOMALT *and* milk may prove misleading. The actual analysis of vitamin-mineral rich COCOMALT (determined by monthly bio-assay) is so well controlled that it is constant at *all* seasons.

The rich full flavor of COCOMALT is an added incentive to both young and old to drink milk. Quick energy . . . body-building nutrients are all present in this malted food dietonic.

R. B. DAVIS COMPANY
HOBOKEN • NEW JERSEY

THE NEW YORK POLYCLINIC

MEDICAL SCHOOL AND HOSPITAL

(ORGANIZED 1881)

(The Pioneer Post-Graduate Medical Institution in America)

Obstetrics and Gynecology

A full time course. In Obstetrics: Lectures; prenatal clinics; witnessing normal and operative deliveries; operative obstetrics (manikin). In Gynecology: Lectures; touch clinics; witnessing operations; examination of patients pre-operatively; follow-up in wards post-operatively. Obstetrical and Gynecological pathology; regional anesthesia (cadaver). Attendance at conferences in Obstetrics and Gynecology. Operative Gynecology on the Cadaver.

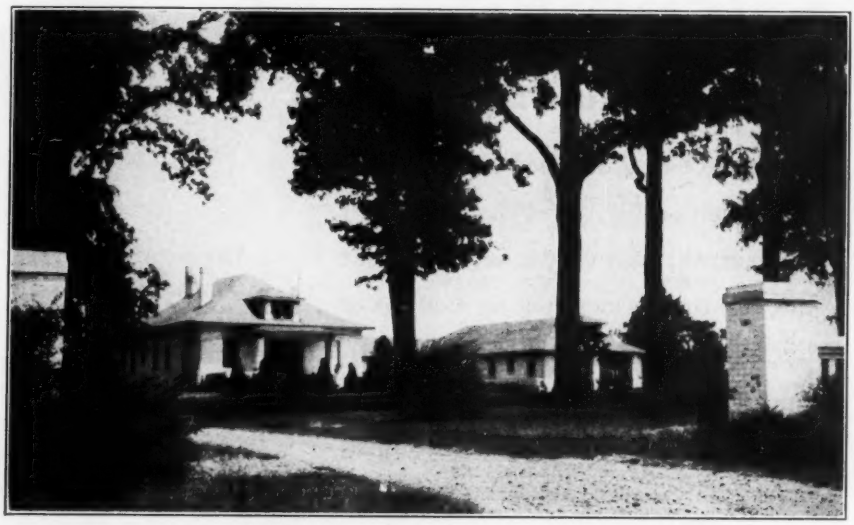
FOR THE

General Practitioner

Intensive full time instruction in those subjects which are of particular interest to the physician in general practice. The course covers all branches of Medicine and Surgery.

FOR INFORMATION ADDRESS

MEDICAL EXECUTIVE OFFICER, 345 West 50th Street, NEW YORK CITY



THE TURNER - GOTTEN SANATORIUM

MEMPHIS, TENNESSEE, Route 6, Box 288

For the Diagnosis and Treatment of Mental and Nervous Disorders

Located on the Raleigh-La Grange Road, five miles east of the city limits. Accessible to U.S. 70 (the Bristol Highway). 53½ acres of wooded land and rolling fields. Equipment new and modern, including the latest equipment for physical and hydrotherapy. Special emphasis is laid upon occupational and recreational therapy under the supervision of a trained therapist. An adequate nursing personnel gives individual attention to each patient.

C. C. TURNER, B.S., M.D., Neuropsychiatrist **NICHOLAS GOTTEN, M.D., F.A.C.S., Neurosurgeon**

THE TUCKER SANATORIUM, INC.

212 West Franklin St. (Corner of Madison)

RICHMOND, VIRGINIA

This is a private Sanatorium for the Neurological Practice of Drs. Beverley R. Tucker, Howard R. Masters and James Asa Shield.

The Tucker Sanatorium is for the treatment of nervous and endocrine diseases. There are departments of massage, medicinal exercises, hydrotherapy and physiotherapy. The Sanatorium is large and bright, surrounded by a lawn and shady walks, large verandas and has a roof garden. It is situated in the best part of Richmond and is thoroughly and modernly equipped. The nurses are specially trained in the care of nervous cases.

Grace Lutheran Sanatorium For Tuberculosis

A Beauty Spot on Prospect Hill

701 South Zarzamora Street
SAN ANTONIO, TEXAS

JAMES L. ANDERSON, M.D., Medical Director

Admits patients irrespective of denomination or creed.

Ideal all year climate.—Excellent medical and nursing care.—Radiographic, Fluoroscopic and Pneumothorax service.

New, distinctive, Individual **Bungalows**, highly modern, and **Private Rooms** with baths and sleeping porches, all equipped with radio.—Beautiful grounds.

Moderate rates.

For booklet and information address:

PAUL F. HEIN, D.D.
Pastor and Superintendent

St. Elizabeth's Hospital
Richmond, Virginia

STAFF

J. Shelton Horsley, M.D., Surgery and Gynecology
John S. Horsley, Jr., M.D., Plastic and General Surgery
Guy W. Horsley, M.D., General Surgery and Proctology
Douglas G. Chapman, M.D., Internal Medicine
Wm. H. Higgins, M.D., Consultant in Internal Medicine
Austin I. Dodson, M.D., Urology
Charles M. Nelson, M.D., Urology
Fred M. Hodges, M.D., Roentgenology
L. O. Snead, M.D., Roentgenology
R. A. Berger, M.D., Roentgenology
Helen Lorraine, Medical Illustration

Visiting Staff

Harry J. Warthen, Jr., M.D., Surgery
W. K. Dix, M.D., Internal Medicine
James P. Baker, Jr., M.D., Internal Medicine
Marshall P. Gordon, Jr., M.D., Urology
Howell F. Shannon, D.M.D., Dental Surgery

Administration

N. E. PATE, Business Manager

The operating rooms and all of the front bedrooms are completely air-conditioned.

School of Nursing

The School of Nursing is affiliated with Johns Hopkins Hospital School of Nursing in Baltimore for a three months' course each in Pediatrics and Obstetrics.

Address: Director of Nursing Education

Laboratory and X-Ray Course

IS NOW TEN MONTHS IN DURATION

Supplemented by Six Months' Practical Work in a Hospital Laboratory, comprising 16 months in all.

COURSE INCLUDES:

Clinical Pathology
Bacteriology
Blood and Urine Chemistry
Hematology
Tissue Sections, Frozen and Paraffin
Serology
Parasitology
Basal Metabolism
Electrocardiography
Roentgenology

A corps of experienced teachers plus completely equipped teaching laboratories covering 3100 square feet.

Write for new catalogue (1940)

Gradwohl School of Laboratory and X-Ray Technique

3514 Lucas Avenue, St. Louis, Missouri
R. B. H. Gradwohl, M.D., Director

Alcoholism
Senility
Drug Addiction

A Modern Ethical Sanatorium at Louisville

Founded 1904

Mental
and
Nervous Diseases

BEAUTIFUL AND SPACIOUS GROUNDS AFFORD OUTDOOR RELAXATION

Our ALCOHOLIC treatment destroys the craving, restores the appetite and sleep, and rebuilds the physical and nervous condition of the patients. Liquors withdrawn gradually; no limit on the amount necessary to prevent or relieve delirium.

MENTAL patients have every comfort that their home affords.

The DRUG treatment is one of gradual reduction; it relieves the constipation, restores the appetite and sleep; withdrawal pains are absent. No Hyoscine or rapid withdrawal methods used unless patient desires same.

NERVOUS patients are accepted by us for observation and diagnosis, as well as treatment.

Select Cases of SENILITY accepted. Physiotherapy—Clinical Laboratory—X-Ray Consulting Physicians

Rates and folder on request

THE STOKES HOSPITAL

Telephones
Highland 2101-2102

E. W. STOKES, M.D., Medical Director, 923 Cherokee Road, Louisville, Ky.

Hoye's Sanitarium

"In the Mountains of Meridian"

MERIDIAN, MISS.

Diagnosis and Treatment of Nervous and Mental Diseases, Alcoholic and Drug Addictions. Especially equipped for the Treatment of Mental Disorders. Convalescents, Elderly People and those requiring METRAZOL THERAPY given special monthly rates. Personal supervision of patients. Consulting physicians.

Dr. M. J. L. Hoye, Supt.
Formerly sixteen years Superintendent of East Mississippi State Hospital

Saint Albans Sanatorium

RADFORD, VA.

A modern, ethical institution, fully equipped for the diagnosis, care and treatment of nervous and mental diseases and selected addiction cases. 2,000 feet elevation. Rates reasonable. Occupational and Hydrotherapy Departments.

J. C. KING, M.D. JAMES KING, M.D.
FRANK A. STRICKLER, M.D.

ALLEN'S INVALID HOME

Established 1890 MILLEDGEVILLE, GA.

For the treatment of

NERVOUS AND MENTAL DISEASES

Grounds 600 Acres — Buildings Brick. Fireproof — Comfortable — Convenient — Site High and Healthful

E. W. ALLEN, M.D., Department for Men
H. D. ALLEN, M.D., Department for Women

Terms Reasonable

DR. MOODY'S SANITARIUM

SAN ANTONIO, TEXAS

315 Brackenridge Avenue Phone: Fannin 5522

For Nervous and Mental Diseases, Drug and Alcohol Addiction and Nervous Invalids Needing Rest and Recuperation

Established 1903. Strictly ethical. Location delightful summer and winter. Approved diagnostic and therapeutic methods. Seven buildings, each with separate lawns, each featuring a small separate sanitarium, affording wholesome restfulness and recreation, in doors and out doors, tactful nursing and homelike comforts.

G. H. MOODY, M.D.
Founder

J. A. McINTOSH, M.D., F.A.C.P.
Superintendent

Dr. Brawner's Sanitarium

SMYRNA, GEORGIA
(Suburb of Atlanta)

● *For Nervous and Mental Disorders Drug and Alcohol Addictions*

Approved diagnostic and therapeutic methods. Hydrotherapy. Electrotherapy, Massage, X-Ray and Laboratory.

Special Department for General Invalids and Senile Cases at Monthly Rates.

JAMES N. BRAWNER, M.D., Medical Supt.
ALBERT F. BRAWNER, M.D., Resident Supt.

APPALACHIAN HALL

Asheville, North Carolina

An Institution
FOR
Rest,
Convalescence,
the diagnosis and treatment of
NERVOUS
AND
MENTAL DISORDERS, ALCOHOL
AND
Drug Habituation

Appalachian Hall is located in Asheville, North Carolina. Asheville justly claims an unexcelled all year round climate for health and comfort. All natural curative agents are used, such as physiotherapy, occupational therapy, outdoor sports, horseback riding, etc. Five beautiful golf courses are available to patients. Ample facilities for classification of patients. Rooms single or en suite with every comfort and convenience.

For rates and further information write Appalachian Hall, Asheville, N. C.

WM. RAY GRIFFIN, M.D. M. A. GRIFFIN, M.D.

McGUIRE CLINIC

ST. LUKE'S HOSPITAL

Richmond, Virginia

. . . Medical and Surgical Staff . . .

General Medicine:
James H. Smith, M.D.
Hunter H. McGuire, M.D.
Margaret Nolting, M.D.
John P. Lynch, M.D.

Orthopedic Surgery:
William T. Graham, M.D.
D. M. Faulkner, M.D.
J. T. Tucker, M.D.

General Surgery:
Stuart McGuire, M.D.
W. Lowndes Peple, M.D.
W. P. Barnes, M.D.
Philip W. Oden, M.D.

Pathology and Radiology:
J. H. Scherer, M.D.

Roentgenology:
J. L. Tabb, M.D.
C. D. Smith, M.D.

Obstetrics:
H. Hudnall Ware, Jr., M.D.
H. C. Spalding, M.D.

Urology:
Austin I. Dodson, M.D.
Chas. M. Nelson, M.D.

Eye, Ear, Nose and Throat:
F. H. Lee, M.D.

Dental Surgery:
John Bell Williams, D.D.S.
Guy R. Harrison, D.D.S.

WESTBROOK SANATORIUM

Richmond ***Virginia***

TELEPHONE 5-3245

Department for Men:
J. K. Hall, M.D.

Associates:
O. B. Darden, M.D.
E. H. Alderman, M.D.
E. H. Williams, M.D.
Rex Blankenship, M.D.

Department for Women:
P. V. Anderson, M.D.

The institution is situated just beyond the northern border of the city on United States Highway Number 1.

The scope of the work of the Sanatorium is limited to the diagnosis and the treatment of nervous and mental disorders and to the addictions to drugs and to alcohol. It affords also adequate facilities for rest and upbuilding under medical and nursing supervision.

The medical staff devotes its entire attention to the patients in the Sanatorium.

The institution maintains a school for trained attendants in which instruction in the care of the nervous and mentally sick is emphasized.

There are twelve separate buildings for patients, with 150 beds. Such a large group of buildings makes possible the more congenial grouping of patients. Rooms may be had single or en suite, with or without private bath. There are a few small cottages for the use of individual patients.

A comprehensive general physical and nervous examination is made of each patient. A mental examination is made when indicated. The examination is typed and a copy of it is available for the referring physician. Complete dental investigation is a part of the general survey.

A skilled teacher gives practical daily instruction to small groups in the arts and crafts. Helpful and interesting occupation in the out-of-doors is made possible for the men patients in the vegetable and flower gardens, on the truck farm, in the poultry yards, and in the dairy.

There are bowling, tennis, croquet and pool. On Sunday evening there is chapel service.

Detailed information is available for physicians.

STUART CIRCLE HOSPITAL

Richmond, Virginia

Medicine:
ALEXANDER G. BROWN, JR., M.D.
OSBORNE O. ASHWORTH, M.D.
MANFRED CALL, III, M.D.
M. MORRIS PINCKNEY, M.D.
ALEXANDER G. BROWN, III, M.D.

Obstetrics:
GREER BAUGHMAN, M.D.
BEN H. GRAY, M.D.
WM. DURWOOD SUGGS, M.D.
SPOTSWOOD ROBINS, M.D.

Ophthalmology, Otolaryngology:
CLIFTON M. MILLER, M.D.
R. H. WRIGHT, M.D.
W. L. MASON, M.D.

Pediatrics:
ALGIE S. HURT, M.D.
CHAS. PRESTON MANGUM, M.D.

Surgery:
CHARLES R. ROBINS, M.D.
STUART N. MICHAUX, M.D.
ROBERT C. BRYAN, M.D.
A. STEPHENS GRAHAM, M.D.
CHARLES R. ROBINS, JR., M.D.

Urological Surgery:
JOSEPH F. GEISINGER, M.D.
FRANK POLE, M.D.

Oral Surgery:
GUY R. HARRISON, D.D.S.

Pathology:
REGENA BECK, M.D.

Roentgenology and Radiology:
FRED M. HODGES, M.D.
L. O. SNEAD, M.D.
R. A. BERGER, M.D.

Physiotherapy:
ELSA LANGE, B.S., Technician
MARGARET CORBIN, B.S., Technician

Medical Illustrator
DOROTHY BOOTH

Stuart Circle Hospital has been operated twenty-seven years, affording scientific care to patients in General Medicine, Surgery, Obstetrics and the various medical and surgical specialties. Detailed information furnished physicians.

CHARLOTTE PFEIFFER, R. N., Superintendent

CITY VIEW SANITARIUM

For MENTAL and NERVOUS DISEASES and ADDICTIONS

Established in 1907

AN ENTIRELY NEW PLANT ERECTED IN 1922

Separate buildings for men and women, ideally arranged and equipped with every facility for the comfort, care, and treatment of the class of patients received.

It is upon the character of service rendered, rather than upon physical facilities that the reputation of such an institution must rest, and to give every patient the maximum of individual attention and unremitting care at all times is the basic principle of our work. An efficient organization exists in all departments. There is maintained an abundantly sufficient staff of capable nurses, divided into day and night shifts, assuring to every patient constant service through each of the twenty-four hours of the day. At midnight this service is as real as at midday.

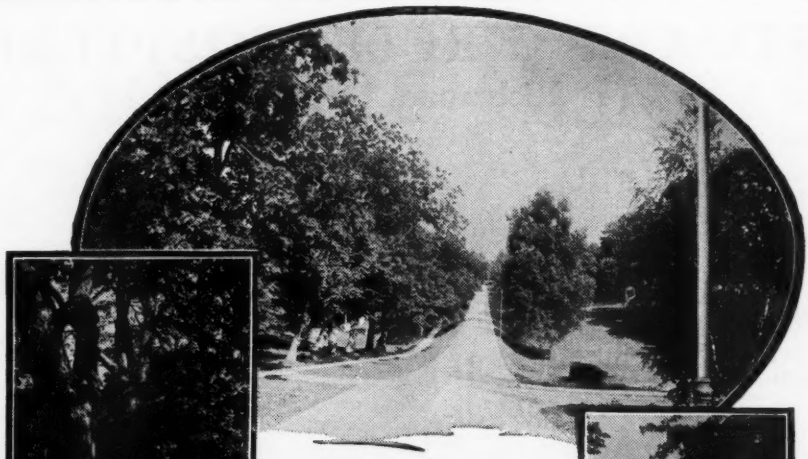
Situated in the midst of a fifty-acre tract and surrounded by a large grove and attractive lawns.

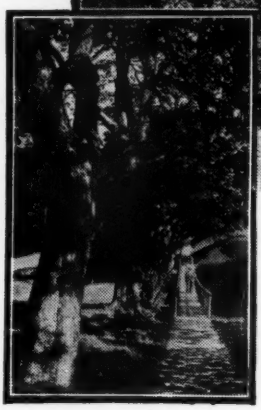
JOHN W. STEVENS, M.D.
Founder

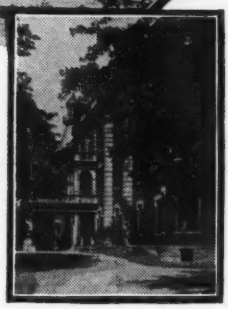
WILL CAMP, M.D.
Medical Director

NASHVILLE R. F. D. No. 1 TENNESSEE

Reference: The Medical Profession of Nashville







The

Cincinnati Sanitarium

Inc. 1873

For Mental and Nervous Diseases

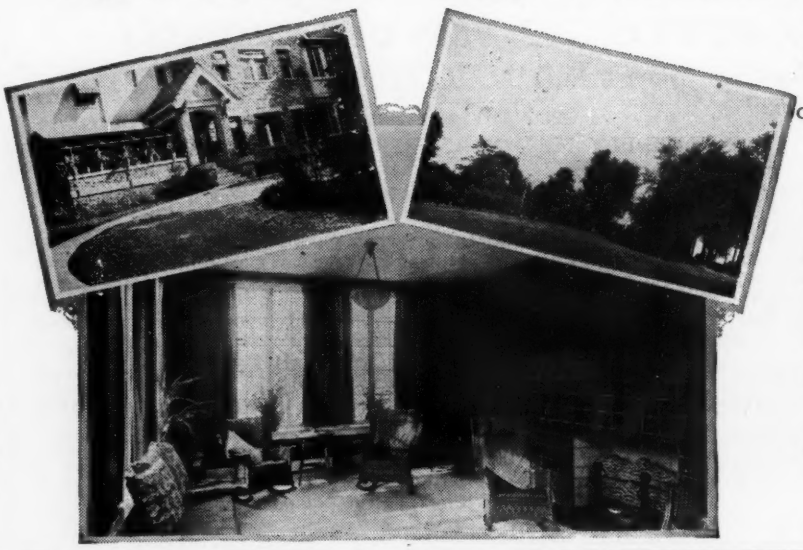
A strictly modern hospital fully equipped for the scientific treatment of nervous and mental affections. Situation retired and accessible. For details write for descriptive pamphlet.

Emerson A. North, M.D.
Charles Kiely, M.D.
Visiting Consultants

D. A. Johnston, M.D.
Medical Director

H. P. COLLINS, Business Manager
Box No. 4, College Hill
CINCINNATI, OHIO

"REST COTTAGE" College Hill, Cincinnati, Ohio



For purely nervous cases, nutritional errors and convalescents.

Completely equipped for hydrotherapy, massages, etc.

Cuisine to meet individual needs.

Emerson A. North, M.D.
Charles Kiely, M.D.
Visiting Consultants

D. A. Johnston, M.D., Medical Director

H. P. Collins, Bus. Mgr., Box No. 4, College Hill, Cincinnati, Ohio

HILL CREST SANITARIUM

FOR NERVOUS AND MENTAL DISEASES AND ADDICTIONS

Metrazol and Insulin Therapy used in Selected Cases. Gradual Reduction Method used in the Treatment of Addictions

Established in 1925

Thoroughly modern in architecture and construction. Eight departments—affording proper classification of patients. All outside rooms attractively furnished. Several bathrooms and rooms with private bath on each floor. Also a spacious sun parlor in each department. Located on the crest of Higdon Hill, 1050 feet above sea level, overlooking the city, and surrounded by an expanse of beautiful woodland. Ample provision made for diversion and helpful occupation. Adequate night and day nursing service maintained.

JAMES A. BECTON, M.D., Physician-in-Charge

P. O. Box 2896, Woodlawn Station, Birmingham, Ala. **Phones 9-1151 and 9-1152**

References: Medical profession of Birmingham and Birmingham Chamber of Commerce.

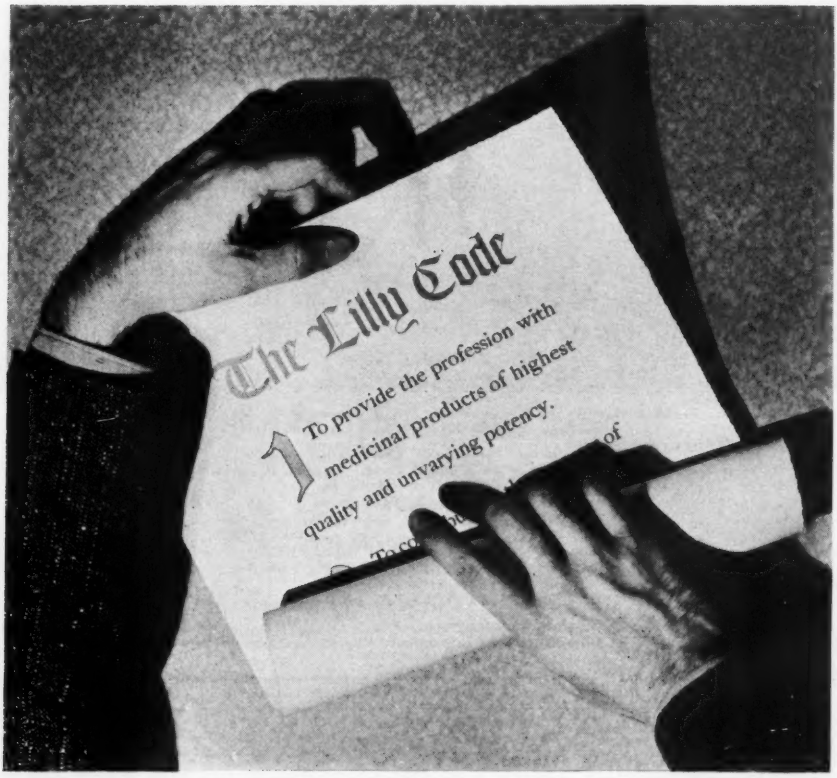
LEONARD D. WRIGHT, M.D.
Medical Director

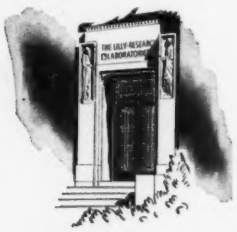
WALTER R. WALLACE
Business Manager

THE WALLACE SANITARIUM

MEMPHIS **TENNESSEE**

For over thirty years in successful operation; just eight miles from the heart of the city, in a quiet suburb, occupying sixteen acres of beautiful grounds, this Sanitarium is especially equipped for the treatment of drug addiction, alcoholism, nervous, and mental disorders, the care of patients requiring metrazol and insulin therapy and is ideal for convalescents.





Orally Administered Bismuth in the Treatment of Syphilis

Pulvules Sobisminol Mass, Lilly*, in a dose of two or three pulvules three times daily, rapidly produce a high urinary bismuth excretion and exert a powerful antisyphilitic effect. To guard against inadequate treatment through irregularity of administration, Sobisminol Mass may best be regarded as an adjunct to parenteral therapy.

A convenient test kit for determination of urinary excretion of bismuth is available.

*Contains a complex organic bismuth compound resulting from the interaction of sodium bismuthate, tri-isopropanolamine, and propylene glycol.

ELI LILLY AND COMPANY

PRINCIPAL OFFICES AND LABORATORIES • INDIANAPOLIS, INDIANA, U. S. A.

SOUTHERN MEDICAL JOURNAL
JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION
PUBLISHED MONTHLY BY THE SOUTHERN MEDICAL ASSOCIATION AT BIRMINGHAM, ALA.

Volume 33 · JUNE 1940 · Number 6

CARCINOMA OF THE LUNG*

AN ANALYSIS OF 195 CASES WITH A SPECIAL NOTE ON NEEDLE PUNCTURE BIOPSY

By C. J. TRIPOLI, M.D.
New Orleans, Louisiana
and
LANG F. HOLLAND, M.D.
Austin, Texas

The advent of lobectomy and pneumonectomy and their development into practical surgical procedures have entirely changed the outlook in many cases of carcinoma of the lung, a disease in which until recently the prognosis was utterly hopeless in all cases.[1] What surgery or radiotherapy can achieve, however, depends entirely upon prompt and accurate diagnosis during the stage in which the selected therapeutic procedure is most likely to be successful. Carcinoma of the lung offers the clinician a fascinating problem in differential diagnosis, the interest of which is often offset by the very discouraging results of treatment. The reason for this paradox is clear: diagnosis is not established in most instances until late in the disease, when therapy is seldom of any avail. Furthermore, the treatment of carcinoma of the lung entails such serious consequences at any stage of the disease that the physician is right in demanding positive diagnostic proof before submitting his patient either to so-called conservative radiotherapy or to radical surgical measures.

In reviewing the recorded series of carcinoma of the lung one is impressed by three considerations: (1) the universal increase in the frequency of the disease in recent years; (2) the uniformity of the general clinical picture; (3) the striking individual variations in the initial symptoms. Part of the increase in the incidence is undoubtedly more apparent than real. More cases are being reported because diagnostic facilities are constantly improving and more cases are thus being recognized. On the other hand, lung cancer is no exception to facts which hold for all varieties of malignant disease, namely, that an actual as well as an apparent increase in incidence is reported by practically all observers, and that increasing longevity predisposes to an increase in the frequency.

INCIDENCE

The fact that carcinoma of the lung represents at the present time approximately 10 per cent of all malignant tumors[2] considerably augments its importance. The reported incidence varies from 8 to 12 per cent. At Charity Hospital of Louisiana in New Orleans, according to a recent report of 74 necropsied cases,[3] it was second in the order of frequency of malignant disease studied, being preceded only by carcinoma of the stomach, of which, over the period surveyed, 150 cases occurred.

The study which we are reporting herewith is based on 195 cases of primary carcinoma of the lung (including the 74 cases just mentioned) which were observed in the same institution from January 1, 1918, to July 1, 1938. Only those cases are included in which the clinical diagnosis was confirmed by roentgenologic examination, bronchoscopic examination, necropsy, or all three methods. Undoubtedly during these years many unrecognized cases occurred, and the true incidence is probably considerably higher than we are reporting.

During the twenty-and-a-half-year period under discussion 576,810 patients over 12 years of age were admitted to Charity Hospital in New Orleans, of whom 321,709 were white (157,189 male, 164,520 female) and 255,101 negro (109,014 male, 146,087 female). The increasing frequency of carcinoma of the lung, whether ap-

*Read in Section on Medicine, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

*From the Department of Medicine of the School of Medicine of Louisiana State University and Charity Hospital of Louisiana at New Orleans.

parent or real, is clear from *Table 1*, which shows an incidence of only nine cases in the first ten years of this study against an incidence of 186 cases during the last 10½ years.

Table 1

TOTAL NUMBER OF CASES, 195

YEARLY DISTRIBUTION IN 195 CASES OF PRIMARY CARCINOMA OF THE LUNG

Year		Year	
1918	1	1929	5
1919		1930	6
1920	1	1931	14
1921		1932	11
1922		1933	16
1923	2	1934	26
1924	1	1935	26
1925	1	1936	20
1926	3	1937	23
1927		1938	34
1928	5		

One hundred thirty-two of the 195 cases of carcinoma of the lung occurred in white patients (118 male, 14 female) and 63 in negroes (53 male, 10 female). The white incidence is thus more than twice the negro incidence and the male incidence is more than seven times the female incidence, which corroborates the trend in all reported series.

Table 2

RACE AND SEX INCIDENCE IN 195 CASES OF PRIMARY CARCINOMA OF THE LUNG

White	130	White males	116
Colored	65	White females	14
Males	171	Colored males	55
Females	24	Colored females	10

The largest number of cases (74) occurred in the sixth decade, which again corroborates the trend of the reported series (*Table 3*). The majority of cases in white females (seven of 14) occurred in the seventh decade.

Table 3

AGE RANGE IN 195 CASES OF PRIMARY CARCINOMA OF THE LUNG

Age	White Male	White Female	Colored Male	Colored Female
30-39	1	1	2	
40-49	20	2	13	2
50-59	41	2	24	6
60-69	38	7	14	2
70-79	16	2	2	
Total	116	14	55	10

ETIOLOGY AND CLASSIFICATION

The etiology of carcinoma of the lung is still not clear. The factors most frequently emphasized include dust, chemicals, gases, fumes and tobacco, as well as such pre-existing diseases as influenza, tuberculosis, and syphilis. The carcinogenic properties of silica and road dust, with and without tar, have been demonstrated in mice by Campbell,[4] and their effects in humans seem to be supported by the reports of Schmorl[5] and of Pirchan and Sikl.[6] The widespread incidence of influenza, and the equally general use of tobacco, suggest a possible relationship, but the association is not clear, and neither these nor any other factors could be demonstrated as causal in any of the cases in our series.

According to most reports carcinoma of the lung occurs most frequently in the upper lobe and on the right side. In the series reported by D'Aunoy and his associates, 38 of the 74 necropsied cases occurred on the right and 36 on the left side, and in 35 instances the primary growth was situated in one bronchus or the other. There is no general agreement as to the pathogenesis, chiefly because of the confusion caused by differences in terminology.

A classification based on gross appearances or one based on whether or not the tumor is primarily cellular or fibroplastic is not so satisfactory as one based primarily on cell type. The so-called "oatcell" tumors, for example, which were once classified as sarcomatous have been proven to be carcinoma. The classification advanced by Fried[7] and modified by Halpert[8] has the advantages of simplicity and of a genetic basis. It includes three groups, reserve cell, columnar cell and squamous cell carcinoma. Thirty-seven of the 74 necropsied cases reported from Charity Hospital were squamous cell, 21 reserve cell and 16 columnar cell.

A word should be said here concerning the superior sulcus tumors which are usually associated with muscular paralysis of the corresponding arm and a Horner's syndrome. Pancoast[9] first described these tumors. Jacox and Baker,[10] as well as others, have presented evidence that they are primary bronchiogenic carcinomas arising at or near the apex of the lung, a possibility which Pancoast himself also suggested. No tumor of this type was observed in this series.

SYMPTOMATOLOGY

It is generally stated that the chief symptoms of carcinoma of the lung, in the order of fre-

quency, are cough, hemoptysis, expectoration of "currant-jelly" sputum, and chest pain, but in the 195 cases we are reporting the order was somewhat different. Chest pain and cough were the chief symptoms, being present, respectively, in 70.4 and 70.3 per cent of all cases. Hemoptysis was present in 57.4 per cent, but persistent expectoration was less frequent, appearing in only 34.3 per cent. Dyspnea was noted in 38.9 per cent and fever in 17.8 per cent.

In the 146 cases reported by Frissell and Knox,[11] cough and pain were present, respectively, in 91 per cent and 71.7 per cent. Hruby and Sweany[12] consider the symptoms as a triad, with cough, pain and dyspnea forming the component parts and the less frequent symptoms included under each heading. The pain may vary in intensity from a boring feeling or a sense of oppression to the excruciating, knife-like pain typical of acute pleurisy.

Anorexia and loss of weight are symptoms which are not seriously considered by some authors, who suggest that weight loss is slight and does not occur until very late in the disease. This does not hold true for our series, in which the average weight loss over a six-months period was 40 pounds in negroes and 30 pounds in white patients. The greatest weight losses were 70 pounds in a negro and 45 pounds in a white patient, both within a three-months period. The least weight losses were seven pounds in a negro and 10 pounds in a white subject, both within a six-months period. Almost 75 per cent of the white patients had lost 20 pounds or more within six months.

As many authors have pointed out,[13] the protean character of the symptomatology of carcinoma of the lung can be readily understood if differences in the location of the tumor and the stage of the disease process are taken into consideration. Tumors situated in the main bronchi, for instance, usually give rise to pain, cough and hemoptysis, whereas tumors located peripherally frequently give rise to no pulmonary symptoms until long after distant metastases have occurred. Dyspnea and the cyanosis which frequently accompany it are due to bronchial obstruction, which may be complete or partial. These symptoms are particularly prominent in partial bronchial obstruction and can readily be explained on the basis of the anoxemia produced by the flow of blood through a partially atelectatic lung. When complete bronchial obstruction is present, on the other hand, cyanosis is not usually observed because the blood is shunted off to well-aerated lung tissue and does not pass through the atelectatic area.

The presence of fever and night-sweats depends upon coexistent infection and not upon the tumor *per se*. If a lung lesion is present, the absence of fever is of diagnostic significance. Hoarseness, aphonia, weakness, dysphagia, such evidences of circulatory disturbance as clubbed fingers, and metastases to the brain, bones, and other sites, may all be part of the picture, but are of relatively little diagnostic value at the period in which therapy would be of the greatest benefit.

PHYSICAL FINDINGS

It is generally agreed that there are no notable physical findings in early carcinoma of the lung. In fact, the signs commonly attributed to the disease are due to bronchial obstruction, and are usually seen late. In the earlier stages, instead of signs of consolidation such as increased breath sounds and bronchial breathing, which might be expected in tumors, there are found signs of atelectasis, such as diminished or absent breath sounds. Other physical signs, such as the presence of pleural exudates or transudates, abscess or bronchiectasis, and so-called unresolved pneumonia or insidious pneumofibrosis, are the result of the malignant process and not signs of the disease itself. The physical findings in our series present no notable exceptions to these observations, although a special word is necessary concerning pleural effusions.

Their diagnostic value is by no means as significant as might be supposed. There is a great deal of truth, however, in the statement that bloody pleural fluid in a patient in the cancer age group is highly suggestive of malignancy of the lung. Effusions are more frequently observed in association with tumors situated near the pleura, and both serous and sanguineous pleural fluid tends to occur rather late in the disease. Thirty-four patients in our series had bloody pleural fluid, although carcinomatous cells could be demonstrated in the aspirated material in only three cases. They could be demonstrated in only one of the eight cases in which straw-colored pleural effusions were present. They were also demonstrated in the sputum in one case.

DIAGNOSTIC PROCEDURES

Roentgenologic Methods.—Of the various diagnostic procedures employed in carcinoma of the lung, roentgenologic study is the most prac-

tical and the most widely used. Of the 80 patients in our series upon whom permission for complete necropsy was granted, 45 had had one or more x-ray examinations at some stage of the disease, and in 19 of these cases a correct diagnosis was possible. On the other hand, the reports in the remaining 26 cases in this group make clear the difficulty of distinguishing between pulmonary malignancy and such other thoracic conditions as aneurysmal dilatation of the arch of the aorta, lung abscess, pneumonia, pleural effusion, infarction, and metastatic lung tumors.[14] As Holman[14] has pointed out, lung abscess and other acute inflammatory processes may so closely simulate carcinoma of the lung that absolute clinical differentiation is often impossible.

Bronchoscopy.—Bronchoscopy is a very effective method of directly visualizing bronchial tumors, especially those in the first and second divisions of the lower bronchi. It also facilitates biopsy of the tumor. Overholt,[15] Jackson and Konzelmann[16] and Taquino[17] have repeatedly pointed out that this method offers a direct means of diagnosing early carcinoma of the larger bronchi or the main subdivisions, in which, according to the necropsy study of D'Aunoy and his associates, more than 50 per cent of all lung cancers are situated. The success of the method depends upon the technical ability of the individual operator, but the technic is now well established and is almost universally available. This method was used in 27 cases in our series, in six of which the tentative diagnosis of primary carcinoma of the lung was confirmed by biopsy.

Thoracoscopy.—This method, valuable as it is for the separation of pleural bands and adhesions in order to facilitate unilateral pneumothorax in tuberculosis, has a very limited field in carcinoma of the lung. It can be used only in peripherally located tumors, which are rather infrequent, but in which it supplies a direct method of visualizing the lung surface and portions of the entire pleural cavity. It cannot be used when the pleural cavity has been obliterated. Biopsy of lung tumors by this method, moreover, is a most formidable procedure and can be employed only in the few cases of malignancy of the visceral or parietal pleura in which the lung cavity remains unobliterated.

Punch Biopsy.—For the last year we have been employing punch biopsy[18-21] of superficially located tumors as a diagnostic method, and have repeatedly demonstrated the efficacy by which biopsy material can be thus obtained. The application of this method to tumors situated at or near the pleural surface of the lung suggested itself to us some months ago, and we believe that it is a practical diagnostic procedure in this limited group of cases.

We use a needle manufactured by the McGregor Instrument Company (Vim-Silverman[22] biopsy needle). The instrument, which operates on the principle of a trocar, consists of a short, hollow outer needle, with a beveled edge, containing a smaller-bore hollow needle. The inner needle is longer than the outer needle and is divided in the center. The cutting edge of the inner needle is beveled in the shape of a V. The technic consists of little more than the simple insertion of the two needles, one within the other, in the same manner as an aspirating needle would be inserted. Local anesthesia is used, and a small incision is made in the skin before the needle is inserted, both to facilitate its entrance through the chest wall and to eliminate the possibility of including skin in the biopsy specimen, which might lead to an incorrect diagnosis of squamous cell carcinoma. The operator should practice punch biopsy on the liver of the cadaver before attempting to employ it in thoracic neoplasms, and thus learn to appreciate "the feel" of lung tumor tissue.

Certain precautions are necessary in the use of this method and certain possible dangers must be pointed out. The proper selection of cases is the first principle of both safety and success. Tumors in the trachea, the bronchi, or the primary bronchial subdivisions, which are readily accessible through a bronchoscope, should not be subjected to puncture through the chest wall. The dangers of such a procedure applied to tumors situated at or near the hilum of the lung are too obvious to need discussion. In short, punch biopsy is applicable only to tumors situated in the periphery of the lung near the pleural surface, and the site of puncture should be the point at which the lung tumor is most superficial, this location having been determined by the taking of radiographs in various positions.

Even in carefully selected cases, furthermore, the risk of air embolism, infection of the pleural cavity, and spontaneous atelectasis is present, just as it is always present in therapeutic pneumothorax. In addition, the risk of hemorrhage can never be ignored. We have no desire to overemphasize these possible dangers, but it is

important to realize that they are always present and that they may be augmented by poor technic in the performance of the puncture.

This typical case demonstrates the observation that tumors of the smaller division bronchi in the upper lobe which are not easily accessible to the bronchoscope may be accessible to needle puncture biopsy as a diagnostic aid.

CASE REPORT

J. A. D. (Hospital No. L-39-39212), a white man, aged 59 years, was admitted to the Charity Hospital of Louisiana on August 19, 1939, with a chief complaint of cough and pain in the right upper chest. The present illness dates back to one year earlier. At that time the patient complained of pain in the upper part of the right chest, anteriorly and posteriorly, aggravated by paroxysms of coughing. There had been a low grade fever which occurred periodically. During the previous month he had coughed up a blood-streaked sputum, and on several occasions about a teaspoonful of bright red blood. He had lost 21 pounds of weight during the preceding year. Review of his systems revealed slight dyspnea on exertion and slight edema of the ankles during the previous two months. There had also been occasional nausea and vomiting, associated with an anorexia during his illness.

The physical examination revealed a fairly well developed, poorly nourished white man, not acutely ill, complaining of pain in the right upper chest with associated paroxysms of coughing. His blood pressure was 125/72, temperature 98.6° F., pulse 76, respiratory rate 22, and weight 115 pounds. There was slight deviation of the trachea to the right and diminished expansion of the right upper chest, with dullness on percussion and diminished to absent breath sounds throughout this area. Slight clubbing of the fingers was noted.

Laboratory examinations showed blood Wassermann negative. The blood picture revealed a moderate normocytic normochromic anemia. Urinalysis revealed no notable findings. Repeated sputum examinations were negative for acid-fast bacilli. Roentgenographic examination was done August 25, 1939. Views of the chest showed atelectasis and passive congestion of the upper lobe of the right lung, believed most probably due to a bronchiogenic carcinoma in the right upper lobe. Bronchoscopy August 26 revealed an obstruction of the right upper bronchus, two-thirds occlusion. Some bleeding was noted. Biopsy tissue could not be obtained. Puncture biopsy was performed August 31. Histologic examination of the biopsy specimen revealed "papillary adenocarcinoma." Repeated bronchoscopy September 1, 1939, revealed tumor mass occluding the right upper bronchus. Biopsy was obtained through the bronchoscope and histologic examination revealed adenocarcinoma. The patient refused surgical removal.

As seen in *Fig. 1*, the tissue obtained by puncture biopsy has not lost any of its histologic characteristics. The breaking up of the tissue structure as seen in specimens obtained by means of a needle and suction syringe is usually not present.

Fig. 1
Punch biopsy of lung adenocarcinoma.

SUMMARY

(1) An analysis of 195 cases of primary carcinoma of the lung is presented.

(2) Carcinoma of the lung now represents 10 per cent of all malignant tumors, improved diagnostic methods having resulted in a marked increase in the frequency of recognition.

(3) The incidence in whites is more than double the negro incidence, and the male incidence seven times higher than the female. The largest number of cases occurs in the sixth decade of life.

(4) The etiology is unknown. The classification into reserve cell, columnar cell, and squamous cell carcinoma is believed to be most reasonable.

(5) Chest pain, cough, hemoptysis, loss of weight, dyspnea, persistent expectoration, and fever are the chief symptoms in the order of frequency. There are no notable physical signs, although atelectasis and pleural effusion are often present. Most physical signs are the result of the malignant process and not signs of the disease *per se*.

(6) Roentgenologic examination, bronchoscopy, bronchography and thoracoscopy are all

useful diagnostic methods, though the latter has a very limited field.

(7) Punch biopsy, although limited to tumors situated at or near the periphery of the lung, is a useful diagnostic aid when it is properly employed.

REFERENCES

1. Ochsner, A.; and DeBakey, M.: Primary Pulmonary Malignancy: Treatment by Total Pneumonectomy. Analysis of 79 Collected Cases and Presentation of 7 Personal Cases. Surg., Gyn. & Obst., **68**:435-451, 1939.
2. Jaffe, R. H.: Primary Carcinoma of Lung: Review of 100 Autopsies. Jour. Lab. & Clin. Med., **20**:1227-1237, 1935.
3. D'Aunoy, R.; Pearson, B.; and Halpert, B.: Carcinoma of the Lung. An Analysis of 74 Necropsies. Amer. Jour. Path., **15**:567-578, 1939.
4. Campbell, J. A.: Cancer of the Human Lung and Animal Experiment. Jour. Indust. Hyg. & Toxicol., **19**:449-462, 1937.
5. Schmorl, G.: Ueber den Schneeberger Lungenkrebs. Verhandl. d. Deutsch. path. Gesellsch., **19**:192, 1923.
6. Pirchan, A.; and Sikl, H.: Cancer of Lung in Miners of Jachymov (Joachimstal). Report of Cases Observed in 1929-1930. Amer. Jour. Cancer, **16**:681-722, 1932.
7. Fried, B. M.: Primary Carcinoma of Lung. Bronchiogenic Carcinoma. A Clinical and Pathological Study. Baltimore: Williams & Wilkins Co., 1932.
8. Halpert, B.: Pathologic Aspects of Bronchiogenic Carcinoma. New Orleans Med. & Surg. Jour., **91**:439-441, 1939.
9. Pancoast, H. K.: Superior Pulmonary Sulcus Tumor: Tumor Characterized by Pain, Horner's Syndrome, Destruction of Bone and Atrophy of Hand Muscles. J.A.M.A., **99**: 1391-1396, 1932.
10. Jacox, H. W.; and Baker, M. R.: Primary Apical Lung Cancer Producing the Symptomatology of a Superior Pulmonary Sulcus Tumor: Report of Case. Radiology, **29**:525-529, 1937.
11. Frissell, L. F.; and Knox, L. C.: Primary Carcinoma of the Lung. Amer. Jour. Cancer, **30**:219-288, 1937.
12. Hruby, A. J.; and Sweany, H. C.: Primary Carcinoma of the Lung with Special Reference to Incidence, Early Diagnosis and Treatment. Arch. Int. Med., **52**:497-540, 1933.
13. Weller, C. V.: The Pathology of Primary Carcinoma of the Lung. Arch. Path., **7**:478-519, 1929.
14. Holman, E.; and Pierson, P.: Carcinoma of the Lung Simulating Inflammatory Disease. J.A.M.A., **113**:108-111, 1939.
15. Overholt, R. H.: Clinical Investigation of Primary Malignancy of the Lung: Diagnosis and Operability. Surg. Clins. N. Amer., **17**:895-904, 1937.
16. Jackson, C. L.; and Konzelmann, F. W.: Bronchial Carcinoma. Bronchoscopic Biopsy in a Series of 32 Cases. Jour. Thorac. Surg., **4**:165, 1934.
17. Taquino, G. J.: Value of Bronchoscopy in Bronchiogenic Carcinoma. New Orleans Med. & Surg. Jour., **91**:429-436, 1939.
18. Hoffman, W. J.: New Technic and Instrument for Obtaining Biopsy Specimens. Amer. Jour. Cancer, **15**:212-220, 1931.
19. Martin, H. E.; and Ellis, E. B.: Aspiration Biopsy. Surg., Gyn. & Obst., **59**:578-589, 1934.
20. Wrenn, F.; and Feder, J. M.: A New Instrument for Aspiration Biopsy. Technical Procedure Combining Principles of Tissue Punch and Improved Operation Syringe. Sou. Med. Jour., **32**:320-322, 1939.
21. Carriero, W. P.: A New Type Biopsy Needle. Amer. Jour. Surg., **37**:341-342, 1937.
22. Silverman, I.: A New Biopsy Needle. Amer. Jour. Surg., **40**:671-672, 1928.

DISCUSSION (*Abstract*)

Dr. George J. Taquino, New Orleans, La.—I am not an internist but an otorhinolaryngologist. I wish to bring out the value of bronchoscopic examination in the diagnosis of cancer of the lung.

During the past 20 years, the increase in the incidence of carcinoma of the lung and bronchi has been marked, but whereas intensive studies are in progress on occupational occurrence, sex dominance, and age incidence, most authors have reached the conclusion that the increased number of reported cases is due primarily to advances in diagnostic facilities. Upon this fact, in addition to the development of a closer cooperation of internist, radiologist, pathologist, and thoracic surgeon, may be based two of the most outstanding features which sum up the progress which has been made in recent years on this disease entity.

Primary carcinoma of the lung possesses interesting clinical and pathologic features, the most disconcerting of which is the fact that it frequently has an insidious onset, and the symptoms which might lead to a positive diagnosis often develop late. In addition to this, it exhibits a tendency to mask its presence by simulation of other acute or chronic pulmonary infections. It is obviously essential, then, for the internist, who is generally the first from whom advice is sought, to become conscious of its prevalence and to be constantly on the alert to discern initiating symptoms which may lead him to suspect its presence. It becomes evident that at this point, in spite of a negative x-ray, a bronchoscopy should be done to visualize the tracheobronchial tree and to determine, if possible, the cause of these symptoms.

An early diagnosis is virtually the most important factor toward a favorable outcome in carcinoma of the lung, the first step of which is achieved through teamwork with the internist. Next, if the mortality caused by these neoplasms is to be reduced, every aid to their early detection must be employed and developed. There are several methods in general use, but it must be remembered that in this respect, as in many others, carcinoma of the lung differs little from carcinoma in any other organ, and each method has its advantages and disadvantages, none being effective in the diagnosis of all types and forms of the disease.

It has been generally accepted that bronchoscopy affords the best means of making an early and positive diagnosis of malignant disease of the bronchi and lung, and consequently has led to its more hopeful treatment. Our present roentgenologic knowledge, through a more accurate understanding of the image presented by varying degrees of stenosis, has also made possible, in many instances, the diagnosis of early carcinoma in this region, despite the fact that cancer actually never shows directly in a roentgenogram until it has reached a very advanced stage. The most recent development of the punch biopsy method as a diagnostic procedure opens up new possibilities in the future, but it cannot be said to have reached beyond a very limited group of cases, which restricts its use to superficially located tumors only, at or near the periphery of the lung.

The administration of punch biopsy requires skillful handling for the obvious possible dangers it entails. It should be used only in carefully selected cases, and puncture of the chest wall is definitely contraindicated in tumors which are readily accessible through bronchoscopy. A variance in biopsy reports has been noted in those patients on whom both diagnostic methods have been employed, and the incidence of positives through the punch biopsy technic is still considerably lower than that obtained through bronchoscopy. Statistics quoted by Jackson and other authorities, as well as my own experience, bear out the significant fact that bronchoscopic biopsy will be positive in about 75 per cent of all carcinomas.

Bronchoscopy has traveled a long, tedious path into

the confidence of the general profession, and through a meticulously trained technic has earned the respect in which it is held today. Formerly it was looked upon as a sort of "last resort," and it is still employed as a last resort by some men because there are a number of cases on which I have been asked to do a bronchoscopic examination where I know a diagnosis could have been made much earlier. I have a case in mind of a man who had a cough, pain, and hemoptysis, but a negative x-ray picture. These symptoms continued after he had had two negative x-ray pictures in about fourteen months. I was then asked if I would bronchoscope him. It was revealed that he had a marked atelectasis of the right upper lobe and bronchoscopic examination showed a malignant condition, marked fixation, thickening of the mucous membrane with inflammatory changes. He had passed the stage where anything from a surgical standpoint could be done for him. That is true, not only of this case, but in numbers of others.

Time has proven that the advantages of bronchoscopy so preponderantly outweigh its dangers that it now holds first position as a diagnostic procedure. This means of visualization not only definitely establishes a positive diagnosis, but the location of the growth is determined and the surgeon is aided thereby in selecting those cases which are thought to be best suited for operation. In addition, it assists in giving definite evidence regarding the level at which the lobe or lobes may be amputated to reach the upper limits of the tumor. Of course, bronchoscopy may not determine the extent of the lesion and the possibility of malignancy should not be excluded on the basis of a negative bronchoscopy or biopsy, yet its value in the great percentage of cases cannot be denied.

A negative biopsy does not mean that there is not a carcinomatous condition present. Very often a tumor mass pushing forward will push the normal mucous membrane in front of it, and in taking a bite for biopsy a piece of normal tissue only may be removed. Unfortunately, many men do not send their patients back for a second bronchoscopy, or even a third bronchoscopy, in order that a positive diagnosis may be made. In one of the cases that Dr. Tripoli has reported we did a biopsy through the bronchoscope and a needle puncture. In each instance a positive diagnosis was made. I understand the first time this man was examined bronchoscopically biopsy was negative and he had to be examined again. We had the privilege of examining him a second time and got a positive biopsy on this bronchoscopic examination.

The study of primary carcinoma of the lung is in a stage of rapid and varied development, some phases of which are still baffling, but there are two factors which never vary from their position of prime importance. The first of these is the absolute necessity for cooperation among the internist, radiologist, bronchoscopist, clinical pathologist, and thoracic surgeon. The second comes as a direct result of this cooperation and is the essential early diagnosis of the condition by the development and application of those methods best suited to achieve this end.

Dr. T. K. Lewis, Birmingham, Ala.—A symptom that I have seen in two cases I believe in the future will receive more notice in carcinomas of the lung, and that is paroxysmal hyperpnea. It is a type of breathing somewhat like an exaggerated Biot's breathing. The first case was a case of primary carcinoma, and the other was a metastasis from a carcinoma of the head of the pancreas. After studying these two cases of this type of dyspnea (I am primarily interested in the heart, and it was referred to me because of a supposed dyspnea), I was very much impressed with this symptom. It was rather outstanding, though it had been overlooked, and I feel that perhaps in the future it will receive more notice.

Dr. Tripoli (closing).—The point brought out by Dr. Lewis is well taken. Dyspnea and cyanosis are quite common in lung cancer in the earlier stages. The cyanosis can be explained by the fact that in a partially atelectatic lung area the blood going through is only partially oxidized. After the complete atelectasis has taken place the blood does not pass through this atelectatic area, but is shunted off to well aerated lung tissues, and the cyanosis and dyspnea disappear. The cyanosis and dyspnea are a result of a partial anoxemia. That is what we accept at the present time, but I am now engaged in trying to prove whether the blood supply to a partially atelectatic area is more or less than the blood supply to a completely atelectatic area. I am speaking of the pulmonary circulation, not the broncho-arterial circulation.

THE IMPORTANCE OF X-RAY INTERPRETATION IN THE TREATMENT OF PULMONARY SUPPURATION*

By BRIAN BLADES, M.D.
St. Louis, Missouri

Roentgen's[1] discovery of the x-ray in 1895 and subsequent refinements in radiologic technic made it possible for the first time to detect minimal pulmonary lesions with great accuracy. The introduction of iodized oil by Sicard and Forestier[2] augmented the radiologic possibilities for pulmonary diagnosis by furnishing a method capable of demonstrating the conformation of the bronchial tree in the living patient. Today every experienced physician appreciates the necessity of securing roentgen films in any evident or suspected pulmonary disease. Although accuracy in diagnosis has increased at an exciting rate, therapeutic measures have not kept pace, so that until recent years there was no practical need for precise localization in the majority of pulmonary lesions. For example, before lobectomy became a feasible operation, patients with bronchiectasis were treated by bed rest, pos-

---

*Read in Section on Radiology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

*From the Chest Service of Barnes Hospital and the Department of Surgery, Washington University School of Medicine, St Louis.

tural drainage, and various palliative measures. It was not necessary, therefore, to accomplish exact localization of the situation of the disease. A bronchogram made in the routine postero-anterior projection was sufficient to establish the presence of bronchial dilatations. Once the diagnosis was determined, the program of conservative treatment could be instituted. The modern thoracic surgeon requires more than a bare etiologic diagnosis in planning operative therapy, however, and other information provided by the roentgen films is of the greatest importance to him in establishing the following points:

(1) the indication for surgery in each case; (2) the exact location of the disease in terms of bronchopulmonary segments; (3) the relationship of the lesion to the chest wall; and (4) the optimum time to institute surgical intervention. In the following discussion, the interpretation of roentgenograms in cases of pulmonary suppuration will be considered from a therapeutic or surgical standpoint as contrasted with the ordinary diagnostic interpretation.

Recent dramatic successes of surgery erase any doubt that extirpation of the bronchiectatic lung tissue is feasible and the preferred method of treatment. Graham and I have performed 35 consecutive lobectomies for bronchiectasis with only one death. In 5 cases of universal bronchiectasis occurring in children, total pneumonectomy has been employed with no mortality. Cure of the disease with disappearance of its associated symptoms has consistently resulted when complete removal of the involved tissue has been accomplished. Interpretation of the roentgen studies should therefore envisage the potentialities of surgical therapy and the scope of the operation necessary to effect cure.

For many years, bronchiectasis has been regarded as a disease involving primarily the lower lobes of the lung. This belief is the result of the failure of the conventional single film to convey a three-dimensional concept of the thorax. Surgical localization of bronchiectasis prior to lobectomy cannot be satisfactorily accomplished from a single postero-anterior film, since the bronchial divisions of the right middle lobe and lingula of the left upper lobe overlap those of the corresponding lower lobe. Following the instillation of iodized oil, one may utilize either the oblique projection or a combination of the postero-anterior and lateral projections to determine the precise situation of the disease. During the past 18 months, Dr. Dan Myers and I have reviewed 75 cases of bronchiectasis which have been considered for surgery. We found that in 59 per cent of the cases showing right lower lobe bron-

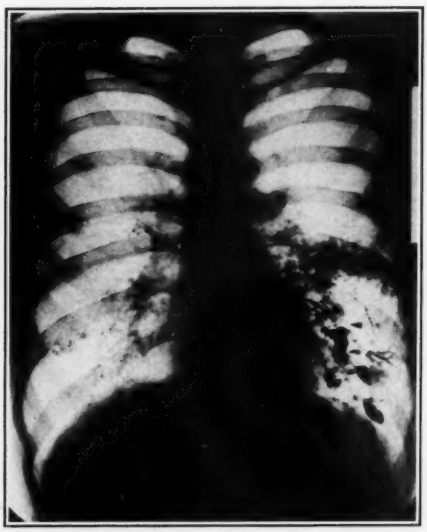


Fig. 1

Conventional postero-anterior bronchogram showing bronchial dilatations in lower left chest. Involvement of the lingula of the left upper lobe might be suspected, but is not established well enough for surgical localization.

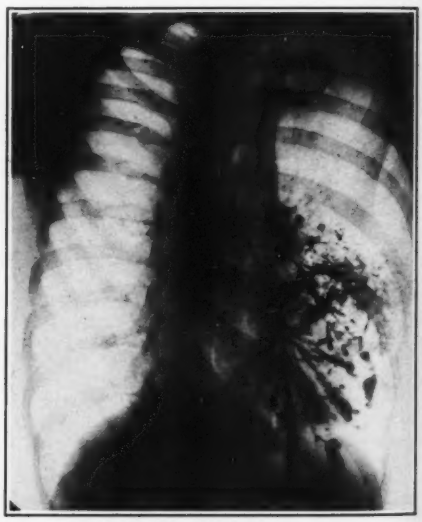


Fig. 2

Right anterior oblique projection on the same case. Note extensive bronchiectasis in lingula of the upper lobe.

chiectasis, the right middle lobe was involved. When the left lower lobe was the principal site of the disease, the lingula of the left upper lobe contained bronchiectasis in 57 per cent of cases. Churchill[3] and O'Brien[4] have commented on the frequency of involvement of the right middle lobe and lingula of the left upper lobe when the corresponding lower lobes are bronchiectatic.

The complete inadequacy of a single posteroanterior bronchogram to determine involvement of the lingula on the left, or the middle lobe on the right, is illustrated in *Figs. 1* and *2*.

The importance of complete extirpation of the bronchial dilatations is obvious. If, for example, a left lower lobe is removed and considerable bronchiectasis remains in the lingula of the left upper lobe, a complete and satisfactory cure cannot be expected. The risk of operation is not materially increased by excising the lingula of the left upper lobe, nor is there any increased danger when the right middle lobe is removed at the time of right lower lobe lobectomy. There is no question that many of the failures of the surgical treatment of bronchiectasis have been the result of faulty preoperative localization, and particularly of a hangover of the conception that bronchiectasis is primarily a disease of the lower pulmonary lobes.

In certain cases, the demonstration of bronchial stenosis may alter the time that operative interference should be instituted. *Fig. 3* demonstrates a stenosis of the left main bronchus. It was apparent that in this case the entire lung was involved with bronchiectasis. The presence of the bronchial stenosis prevented effectual postural drainage through the tracheobronchial tree, and in spite of repeated bronchoscopy, the patient's temperature remained at high levels and it was necessary to perform a total pneumonectomy as a life-saving measure. *Fig. 4* shows the appearance of the patient 21 days after total pneumonectomy. The child is now well and entirely free of symptoms. If the bronchial stenosis had not been present, pneumonectomy would have been delayed with the hope that the infection would subside and the temperature return to a normal level.

For many years the treatment of pulmonary abscess has been a controversial subject. There are many conflicting opinions concerning the optimum time to attack a pulmonary abscess surgically. Arbitrary time limits have been suggested in medical literature by which a lung abscess is designated as chronic after 6 to 8 weeks' duration, and the patient is considered eligible for surgical drainage. These dogmatic criteria are probably necessary to establish a division between acute and chronic processes for the purpose of description, but are not suitable for determining the proper time for surgical intervention in the individual case. The decision when to abandon conservative for radical treatment must depend on clinical impressions and roentgen findings. Each case of pulmonary abscess should have the benefit of a trial of conservative therapy irrespective of the time element. If there is rapid spread of the local lesion as evidenced by clinical and roentgenologic ob-

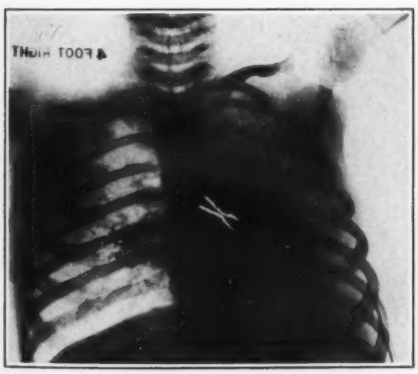


Fig. 3
Bronchogram demonstrating stenosis of left main bronchus and bronchiectasis involving the entire left lung.

Fig. 4
Appearance of patient 21 days after left total pneumonectomy. The child is entirely well and enjoys normal activity.

servation, however, drainage should be instituted regardless of duration of symptoms.

Once it is determined that a lung abscess should be treated by drainage, the most important single point to determine is the proper place to make the incision. If the approach is even slightly inaccurate, pleural adhesions will probably not be encountered or will be insufficiently strong to allow drainage of the abscess in one stage. If an irritating pack must be placed in the wound to create adhesions between the lung and pleura, the patient is faced with a dangerous delay, since evacuation of the abscess must be postponed from 10 days to 2 weeks. Moreover, when the second stage is performed, if the lesion is not directly under the wound, healthy lung tissue will be violated before the abscess can be reached.

It is usually possible to obtain a fairly accurate conception of the location of a pulmonary abscess with conventional postero-anterior and lateral roentgenograms. Body section laminagraphy, invented by Jean Kieffer and developed by Sherwood Moore,[5] has been very useful in the surgical localization of pulmonary suppuration. Not only does the laminagram give the exact level of the abscess measured in centimeters from the chest wall, but not infrequently multilocular lesions are demonstrated which cannot be detected on conventional roentgenograms. *Figs. 5* and *6* illustrate the value of the laminagram in surgical localization of pulmonary abscesses.

It is appropriate that the importance of the superior divisions of the lower lobes and their roentgenologic identification be mentioned in connection with the surgical management of pulmonary suppuration. Levitin and Brunn[6] described the superior divisions of the lower lobes and their peculiar anatomical and embryologic features. They also mentioned that this particular segment of the lung is a frequent site of the disease. An analysis of 69 cases of pulmonary abscess treated in the Chest Service at Barnes Hospital revealed that 47 per cent of all abscesses of the lower lobes were situated in their superior portions. The practical importance of the identification of pulmonary suppuration in this location is that an incorrect diagnosis of central abscess may be made. For many years, authoritative opinion has classified lung abscesses as peripheral and central, depending on the relationship to the large bronchi and hilum of the lung. In the past and even at the present time, artificial pneumothorax is recommended for the treatment of central abscesses which are considered inaccessible for surgical drainage. If a lesion of the superior division of the lower lobe is mistaken for a central abscess, institution of artificial pneumothorax may cause a tear of the abscess wall, which will result in a pyopneumothorax. It is extremely easy to mistake a superior division of the lower lobe lesion for a central one when a single frontal projection is employed. Even when the lateral projection is used, minor errors in radiologic technic, notably

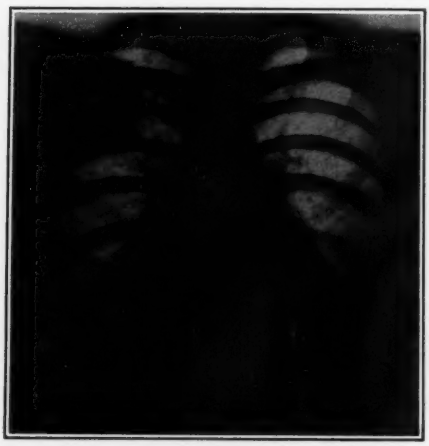


Fig. 5
Conventional roentgenogram of bilateral pulmonary abscesses.

Fig. 6
Laminagram of same patient showing multiple cavitation. Operative confirmation. Abscess in left lower lobe healed following bronchoscopic aspirations, bed rest and postural drainage. Surgical drainage was necessary to cure the abscess in the right upper lobe. The patient is well and free of symptoms.

a rotation in the position of the patient, may give the false impression that the abscess lies in the region of the pulmonary hilum. *Figs. 7* and *8* illustrate the location of an abscess in the superior division of a lower lobe. The concept of central abscess has been questioned by Neuhof and Touroff,[7] who believe that in every instance a pulmonary abscess is peripheral in location. We are inclined to agree with this contention; but regardless of its absolute validity, actual experience has demonstrated that serious consequences may follow the employment of artificial pneumothorax in superior division abscess.

The two major objectives of the various operations advocated in the surgical treatment of lung abscess are: (1) drainage of purulent accumulations through the chest wall, and (2) the excision of the diseased tissue. In our experience compression therapy has been a failure in the management of suppurative disease. The problem in the individual case requiring surgical intervention, therefore, consists in the determination of whether simple external drainage or excision of the involved lobe should be carried out. Two general types of abscess may be distinguished from this viewpoint, those with a single large cavity and those with multiple pockets distributed throughout the major portion of one or more lobes of the lung. It is evident that pneumonotomy, which is a suitable procedure for the drainage of solitary abscesses, will fail in many of the patients having multiple abscess cavities. The patient's clinical condition and other factors may, of course, make the risk of the preferred operation of lobectomy prohibitive in certain cases of multiple abscess formation confined to one lobe. When a pulmonary abscess is of long standing, associated bronchiectasis is frequently present. Simple drainage will not cure the bronchiectasis, and is regularly followed by a persistence of purulent expectoration. It is of paramount importance therefore to employ iodized oil bronchography in the study of chronic lung suppurations, since the demonstration of bronchial dilatations denotes that excision of the diseased lobe is the treatment of choice.

Prerequisite to successful surgical treatment of pulmonary suppuration, either bronchiectasis or lung abscess, is the proper interpretation of roentgenograms. Not only is the correct anatomical approach to the lesion established, but frequently the optimum time for surgical intervention and the proper type of operation can be determined. In addition to conventional roentgenography and bronchography, the radiologic development of laminagraphy is of distinct value in the study of pulmonary suppuration.

REFERENCES

1. Glasser, Otto: Wilhelm Conrad Roentgen and the Early History of Roentgen Rays. Berlin: Springer, 1931; London: Bale, 1933; Springfield: Thomas, 1933.
2. Sicard, J. A.; and Forestier, J.: Methode Generale D'Exploration Radiologique par l'Huile iole (Lipiodol). Bull. et Mem. Soc. Med. d. Hop. de Paris, **46**:468-469, 1922.
3. Churchill, Edward D.: Lobectomy and Pneumonectomy in

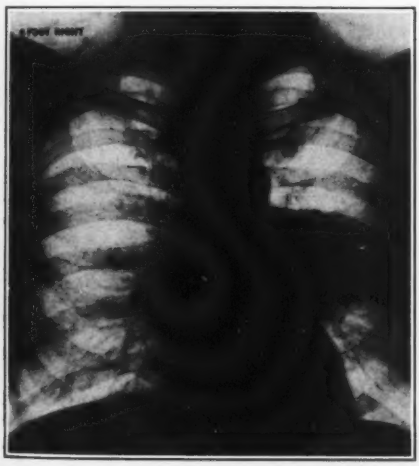


Fig. 7
Postero-anterior projection of chest. Pulmonary abscess of superior division of lower lobe. The impression on frontal view is that the lesion is centrally located.

Fig. 8
Lateral roentgenogram of same case. Note extreme posterior position of abscess and peripheral location easily accessible for drainage.

Bronchiectasis and Cystic Disease. Jour. Thoracic Surg., **6**: 286-311 (Feb.) 1937.
4. O'Brien, E. J.: Results of Fifteen Consecutive One-Stage Lobectomies for Bronchiectasis. Jour. Thoracic Surg., **6**:278-285 (Feb.) 1937.
5. Kieffer, Jean: The Laminagraph and Its Variations, Applications and Implications of the Planigraphic Principles. Amer. Jour. Roent. & Ra. Therapy, **39**:497-513 (April) 1938.
6. Levitin, Joseph; and Brunn, Harold: Study of the Lower Lobe of the Lung: Explanation of Roentgenologic Shadows. Arch. Int. Med., **57**:649-665 (April) 1936.
7. Neuhof, H.; and Touroff, A. S. W.: Acute Putrid Abscess of the Lung. Surg., Gyn. & Obst., **66**:837, 1938.

DISCUSSION (*Abstract*)

Papers of Dr. Robert J. Reeves, Dr. H. B. Mulholland and Dr. Brian Blades. Paper of Dr. Reeves was published in the April issue, page 361; paper of Dr. Mulholland in May, page 482.

Dr. Vincent W. Archer, Charlottesville, Va.—There are one or two things in Dr. Blade's paper which I wish to emphasize. The first is the absolute necessity of careful chest examination. Too many chest examinations are made simply using the conventional stereoscopic postero-anterior films. When we do this, and see a peculiar lesion situated somewhere in the chest, there is an immediate indication for further examination; laterals, obliques, fluoroscopics, kymographic studies as indicated and, more recently, laminagraphic studies. If we resort to these more frequently, we shall miss far fewer chest lesions.

As far as calling them by name after we see them, that is a different matter, as has been demonstrated clearly in Dr. Reeves' paper.

In discussing bronchiectasis, Dr. Blades, of course, has taken up only bronchiectasis as seen by the surgeon. I like to think of bronchiectasis, and our interest in bronchiectasis, as being prevention of an advanced process rather than taking care of it after it has become fully blown and requires surgical intervention.

When we as radiologists see a minor degree of bronchiectasis (if our internists, in sending in their cases, are not sinus-minded or throat-minded) we should bring to their attention that bronchiectasis is frequently the result of long-continued infection above the collar button, with drainage downward, and look for that as a cause.

One of our radiologists, Dr. Wasson, now of Denver, has very beautifully demonstrated in x-raying children's sinuses and chests from birth on up to 16 or 18 years that there is a very definite correlation between the development of sinus disease and so-called bronchosinusitis, which, if untreated, may go on to bronchiectasis.

About two or three years ago the chest group at Mount Sinai in New York presented a very intriguing set of statistics on the radiation treatment of at least the minor to moderate degrees of bronchiectasis by use of small daily doses of radiation over quite a long period of time.

This treatment has not been going on long enough for us to evaluate its end results. Before considering a lobectomy, certainly in case of a moderate degree of bronchiectasis, you have all to gain and nothing to lose by at least trying these small, fractionated doses of radiation. We have tried it in very few cases, but in some of our patients at the University of Virginia we have been quite agreeably surprised with the results that have been obtained. It is not as infallible as Father John's remedy for all types of bronchiectasis, but I believe in a certain percentage it is of definite value.

There is one phase of the diagnosis of lung abscess which should be mentioned, and that is caution in diagnosing central rarefaction in an area of consolidation as beginning lung abscess. So many of us have seen pneumonia that is rather slow in resolving with the central area rarefied. I know my face has been reddened on several occasions by calling this a beginning lung abscess. In this type of case continued examination is necessary before we arrive at a definite diagnosis of lung abscess and advise bronchoscopy or other procedures.

I wish to report a very enlightening and humiliating experience that happened to me very recently. I think sometimes we learn more from our mistakes than we do from the cases in which we make fairly decent diagnoses.

An elderly colored man came into the clinic with the history that he had been perfectly well until about a month before he came in. At that time he had a pain in his chest, which, from his history, sounded like pneumonia. He said his doctor "drew off some water from his chest." He was sent to us with a diagnosis of empyema. We x-rayed his chest with anterior-posterior and laterals and saw at least three different fluid pockets definitely in the pleural cavity and one in his upper mediastinum, with a definite fluid level in it.

We diagnosed these as empyema pockets with a probable mediastinitis or mediastinal abscess. The pockets in the chest were aspirated and fluid was obtained. I very carefully localized the area where the mediastinal pocket should be tapped. The area was aspirated and a couple of hundred c. c. of very glairy mucoid material was obtained which was perfectly evidently coming from the esophagus. I gave the patient a little barium. He had an esophagus that was at least 5-6 cm. in diameter which was the mediastinal pocket.

This case is reported as demonstrating the difficulty in diagnosis in some of these intrathoracic lesions and the necessity of care in correlating everything. If I had gone into the patient's history a little more carefully, I should have learned that he gave a history of difficulty in swallowing since the age of 12 years, but when he got in trouble in swallowing, the Lord told him to drink just water and that would cure him.

Dr. Walter S. Lawrence, Memphis, Tenn.—Thirteen years ago, at the Southern Medical Association meeting in this same building, I presented a patient who had generalized blastomycosis. The lung picture was one that could not be differentiated from tuberculosis, but to help in the diagnosis, the patient had skin lesions on both hands, of blastomycetic dermatitis, and on one foot, a large abscess on his back that had been opened and had drained for a month or more but failed to heal, and an abscess developing over the right shoulder blade.

The causative organisms were recovered from all of these lesions, from the sputum, from the skin lesion, and from the pus draining from the abscess on the back. All of them were loaded with blastomycetes. The patient had been thoroughly saturated with iodides and was steadily losing ground. He was very thin, had no appetite and was bedridden most of the time. I was

doing the x-ray work out there at the time, and insisted upon his having x-ray treatment. X-ray treatment to his hands and his foot speedily healed those lesions.

High voltage x-ray was given through the lungs, but did not bring about improvement.

The patient was sent in an ambulance to my office for ultraviolet treatment, under which he improved immediately.

He was treated every other day for two months, at the end of which time he had gained some ten to fifteen pounds, was a picture of health and, as far as I could see, perfectly well.

A similar case that I saw recovered entirely after a course of sun and sea bathing on the coast of Florida.

Dr. W. W. Robinson, Memphis, Tenn.—I agree with Dr. Blades that pulmonary suppuration amenable to surgical intervention should be accurately localized with reference to the broncho-pulmonary segments involved as well as to its relationship to the chest wall, if the best therapeutic results are to be obtained. I am very glad that he has emphasized the importance of recognition of the suppurative lesions of the superior division of the lower lobes of the lungs versus so-called central abscesses. This introduces the question of etiology of lung abscesses. I agree that most of these are peripherally placed. However, I think the site of an abscess is governed more or less by the mode or method by which infection is introduced into the lung. Aspirated infectious material may produce centrally placed abscesses, whereas blood stream borne infection, that is, the hematogenous or embolic method of abscess production, usually causes peripherally placed lesions.

While Dr. Blades has discussed the interpretation of roentgenograms in these cases purely from a surgical standpoint, I am sure that he will agree that the diagnostic interpretation, or identification, of each and every suppurative lesion of the chest is very important and almost inseparable from its therapeutic indications, as the type of lesion dictates the type of treatment, whether this be surgical, medical, or one of radiation. Of the several suppurative lesions which must be differentiated, may I mention one which may be readily confused with abscess formation, and which may be primarily responsible for the production of bronchiectasis. I refer to primary malignancy of the lung, especially the alveolar or parenchymal type, although some of the infiltrated bronchogenic carcinomas do simulate abscess formation both clinically and roentgenologically. The differential diagnosis, while it will be difficult by the use of the conventional postero-anterior, lateral and stereoscopic radiographs, or even by laminagrams, can readily be made by bronchograms in conjunction with roentgenograms following aspiration pneumothorax. The filling defects in the bronchial tree are visualized by the bronchograms, and the nodulation within the necrosing tumor is demonstrated by the film made after aspiration and the injection of a small quantity of air. The aspirated material may be examined for the presence of tumor cells.

Dr. Charles H. Heacock, Memphis, Tenn.—Dr. Mulholland has cited quite a few cases in which the roentgen ray examination was of great aid in the diagnosis. In most of these the diagnosis rested entirely on the roentgenologic report and the physical findings were either absent or very meager.

Teachers of medicine all through the years have emphasized over and over again to their students that special examinations, such as the roentgen ray, should be used only to confirm the history and physical findings. Without disparaging this teaching or the value of the history and physical examination, we know that many times the roentgen examination gives positive findings when all other methods of examination are negative.

By the employment of the conventional and, in some instances special types of x-ray examination, I believe we can always demonstrate whether or not there is a departure from normal. When we endeavor to interpret these findings in terms of pathology, our percentage of error will probably be as high as the percentage of positive cases in which the internist's findings were negative. The greater percentage of accuracy will be attained and the maximum benefit will result to the patient if the roentgenologic examination is requested more frequently in acute respiratory infections and the internist and radiologist consult in every case.

There has always been some question about the pathogenicity of some of the organisms discussed by Dr. Reeves.

The finding of blastomycosis and actinomycosis, and probably Monilia, in the sputum will be regarded as sufficient explanation when a gross lesion is apparent on the roentgenogram. My impression is that this is not so true of Oidium or Streptothrix.

Recently I saw a patient with an atelectasis of the left upper lobe which I thought was due to a bronchiogenic carcinoma. Bronchoscopic examination and bronchograms did not establish the identity of the lesion, but streptothrix were found in the sputum. After a course that was progressively down hill, the patient died about four months after the onset of symptoms.

I would like to ask Dr. Reeves whether he would regard the Streptothrix as the etiological organism in such a case or as merely an incidental finding.

Dr. Reeves (closing).—Answering Dr. Heacock's question about his case of Streptothrix, I do not believe anyone could tell whether it is due to Streptothrix infection or not. You might have two associated, secondary infections. It is very difficult to be sure about fungus infections.

I might not have made it clear that we do not cure all of these cases. Only a few of the cured cases were shown. Patients with blastomycosis and actinomycosis, as all of you know, as a rule, die. We have very few of the two conditions which are actually cured.

Dr. Blades (closing).—Dr. Archer mentioned the importance of sinus and throat infections in bronchiectasis. Before recommending lobectomy in any case of bronchiectasis, the nasal sinuses should be investigated and treatment instituted if infection is found. The point made about differential diagnosis between early pneumonia and lung abscess is important. It is impossible in many instances to be certain of the exact nature of the lesion until symptoms characteristic of lung abscess are present or evidence of rarefaction of lung tissue is detected on x-ray examination.

Dr. Robinson mentioned another important point, namely, malignancy of the lung causing the symptoms characteristic of pulmonary abscess. This situation is so common that we, for a working basis, consider in every case of pulmonary suppuration in an individual past middle age the possibility of bronchogenic carcinoma. Bronchoscopic examination will often establish the exact diagnosis.

THE BIOLOGIC ACTION OF RADIANT ENERGY*

By EUGENE R. WHITMORE, M.D.
Washington, District of Columbia

III. SUNLIGHT, QUARTZ MERCURY ARC RADIATIONS, AND LESIONS OF THE SKIN

In a previous article,[24] (1929) I have discussed the effect of measured heavy doses of quartz mercury arc radiations and have referred to some of our earlier beliefs regarding the effects of actinic rays, with special reference to life in the tropics; but without any consideration of the prolonged effects on the skin.

Woodruff[24] (1905) discussed the effects of tropical light on white men; and again we find nothing on the prolonged effects on the skin.

(A) CLINICAL OBSERVATIONS

(1) Hyde[8] (1906) discussed the influence of light in the production of cancer of the skin: said that cancer of the skin is less common in the negro than in the white in the United States; that the heat rays are not responsible for the preponderance of cancer of the skin among those exposed in out-of-door occupations, as shown by the rarity of the condition in Africa, Arabia, Egypt, and Syria; cited Law's experience with the rarity of cancer of the skin of miners in a town where cancer of the skin was not uncommon; and he was well aware of the part played by the pigment of the skin in protecting against cancer of the skin.

(2) Lawrence[11] (1912 and 1928) discussed the low humidity and abundant sunshine as a causal factor for cancer of the skin in Australia. The humidity along the coast is about 60 per cent, while inland it is about 30 per cent; and there is a high average number of hours of sunshine. Moisture in the atmosphere impedes the passage of the ultraviolet rays.

In 20,000 patients in private practice of dermatology, from 1908 to 1927, there were 1,374 cases of rodent ulcer (6.82 per cent), 877 cases of keratosis (4.38 per cent), and 395 cases of epithelioma (1.975 per cent). This means that rodent ulcer is over twenty times as frequent in cases in dermatologic practice in Australia as in England.

The French do not willingly accept blonde candidates for government service in hot climates, as they appear to have less resistance to torrid diseases than do dark men. Lawrence suggested testing an individual's skin for ability to form pigment by raying the forearm with an ultraviolet lamp: if there is no pigmentation, the person is not suitable for certain parts of Australia.

One case was a man who lived at Mackay, Queensland (on the coast, where the humidity is higher); he had to go inland (where the humidity is lower) several times a year and stay for some time. He developed a rodent ulcer on the scalp, a squamous cell cancer of the back of the hand, and keratoses on the exposed skin (*Fig. 1*).

Lawrence distinguishes *keratosis senilis* and *keratosis solaris:* the latter develops earlier in life than does the former; basal cell cancer may develop in or around *keratosis senilis,* but squamous cell cancer may develop in *keratosis solaris.*

(3) Molesworth[13] (1927) was attracted by the greater incidence of rodent ulcer in Australia than in England and undertook the study of the reason for this. He notes that the German name for rodent ulcer is "seaman's skin cancer"; and that Darier described "cancer of agriculturalists."

In Australia, rodent ulcer is most common in persons with fair skin, especially persons who freckle. It occurs especially in the Scotch and Irish, probably because of the tendency to red or sandy hair, or brown hair with blue or gray eyes and a very fair clear skin. The Scandinavian and north German types are affected quite out of proportion to their numbers; the English are next, but many of the English are dark, or tan readily. No cases occur in Italians or in Chinese or colored, though many of the latter pursue an outdoor occupation, especially as market gardeners. It occurs on the skin of exposed parts; in persons in the country and those having outdoor occupation, and in indoor persons who have outdoor habits, hobbies, and sports. It occurs in women of a susceptible type of complexion and outdoor habits, who show signs of exposure.

Most of the patients are over 35 years of age (the youngest was 20 years of age: a sandy-haired freckled country boy of Irish-Scotch de-

---

*Read in Section on Pathology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

*From the Department of Pathology, Georgetown University Medical School, Washington, D. C.

Fig. 1

Photograph of man with keratoses, rodent ulcer of scalp, and epithelioma of back of hand. This patient used to sunburn so severely that he would only tuck his sleeves up half way when at work. The keratoses are seen to be limited to the area exposed to the sun's rays (Lawrence).

scent, who had been much exposed from babyhood).

Of 37 patients, 23 were men and 14 women (9 English, 8 Scotch, 9 Irish, 4 mixed Scotch and Irish, 5 Scotch or Irish mixed with English, 2 German). So, 26 had Scotch or Irish blood, entirely out of proportion to the representation of these stocks in the community, as was the case with the two Germans.

All patients in this series were 40 years of age or over; only 10 were under 50 years of age. The preceding keratoses may be evident for some time and rodent ulcer may not appear for several years after the person has quitted undue exposure to the sun.

A family of mixed Irish and English blood contained 3 brothers, 5 sisters. The brothers, all farmers, developed rodent ulcers on precedent lesions; a dark sister and a sister who married at 20 years of age and lived in Sydney, were the only ones to escape.

In Australia, all outdoor occupations are carried on by the whites: a fair race, in a country the greater part in the temperate zone, but singularly cloudless for the greater part of the year; where the men wear clothing similar to that worn in England, wear a narrow-brimmed felt hat, with little or no fear of sunstroke, where work goes on continuously through the middle of the day, under the full blaze of the sun in a cloudless sky for the greater part of the year, and where the mid-day siesta has never obtained. The people scorn precautions against sunburn.

Outdoor occupation plays a part in cancer of the lip, which is usually (99 per cent in Australia) on the lower lip.

Rodent ulcer occurs on the more actively sebaceous parts of the face: the lip, hands, and forearms (where squamous cell cancer occurs) are much less actively sebaceous.

(4) Roffo[17] (1928) drew attention to the high incidence of cutaneous epithelioma in Argentina, localized exclusively on the face and on the backs of the hands. In 5,000 cases of cancer at the Cancer Institute at Buenos Aires, none had cancer on any part of the skin covered by clothing (except in one or two cases where tumors developed in nevi or burn scars). The distribution of 1,500 cases of epithelioma of the skin was as follows:

EPITHELIOMA OF THE SKIN (1,500 CASES)

(a) Regions exposed to the sun	Per Cent	(b) Regions protected by clothing	Per Cent
Skin, face	95.51	Hairy skin	1.02
Skin, back part of the hands	3.07	Foot	0.52

On the face, the parts most affected are those most prominent and exposed: nose, 61 per cent; cheeks, 18 per cent, and hardly any on the forehead. It is more common in men (70.9 per cent) than in women (29.1 per cent). Because women take better care of their skin, protecting it with powder, it occurs only in country women who are of humble standing and do not protect their skin. It develops in workmen and persons of higher social classes who have to expose themselves to the sun all day, as farmers and planters. Those affected generally have a very white skin: Roffo has not seen a single case in natives, negroes, or mulattoes. The appearance is peculiar: the face, up to the brim of the hat, and the hands up to the sleeves of the coat or shirt, present at first a diffuse erythema, and later numerous pigmented areas, which contrast with the white skin of the forehead and forearms. These pigmented areas become more pronounced and hyperkeratotic; then they ulcerate and become cancerous.

(5) Phillips[14] (1939) analyzed the records of over 1,000 cases of cancer of the skin treated in a clinic in Texas during a period of twenty-five years. He found a high incidence of cancer of the skin in persons having an outdoor occupation as compared with indoor workers, and also a predilection for exposed areas of the body.

(6) Drabble[3] (1929) studied skin cancer in cattle in Australia. But he says these lesions are due to sensitization of the unpigmented skin to the action of the sun's rays as a result of eating light-sensitizing plants by the animal; so, consideration of this phase of the subject belongs in the other part of this study (4).

(B) ANIMAL EXPERIMENTATION

(1) Findlay[4] (1928) used epilated white mice, with a quartz mercury vapor lamp whose spectrum was said to cover a range from 2,000 angstrom units in the ultraviolet to 10,140 angstrom units in the infra-red. The bottom of the cage was 18 inches from the burner; he began with one minute daily exposure; after 5 months, 2 minutes daily; and after 2 months more, 3 minutes 4 times a week. Of 20 mice, 4 developed malignant tumors (epitheliomas) on the ears; 3 others developed papillomas on the ears. The shortest time in which he got lesions was eight months. No lesions developed on the epilated regions.

(2) Findlay[5] (1930) used rats, with the same lamp as before, at 18 inches distance, one minute exposure, three times a week. Six hundred and sixteen days after beginning, a small papilloma appeared on the ear of one rat; one month later, two papillomas on the other ear. One month later the rat died of pneumonia. Histologically, the lesions on the ears were papillomas, with no infiltration or metastases.

Did infra-red play a part? A mouse was exposed to a 1,000 watt radiant heat bulb (glass): in 12 months there were no evident lesions. The mercury vapor lamp causes not over 5° rise in temperature in the cage; so the heat rays are not the cause.

The minimum time in the mouse for a lesion to develop was 8 months.

The minimum time in the rat for a lesion to develop was 21 months.

There is a similar difference of time in mice and rats to produce tar cancer.

In man, it takes 10 to 15 years to produce tar cancer of the skin.

In man, it takes at least 15 years to produce a cancer of the skin by sunlight.

So, the species of animal is a very important factor.

(3) Putschar and Holtz[15] (1930) exposed rats to a quartz mercury vapor lamp, with the burner 60 cm. from the bottom of the cage. They started with 2 minutes exposure daily, and rapidly increased the time of exposure, so that at the end of 12 days the exposure was continuous, 24 hours a day: this was continued for 11 months. The rats drank much water; and they became shy, and would bite, perhaps because they always became blind.

After 27 weeks they first got carcinoma of the ears of the rats.

They found no definite relation between color of hair and cancer susceptibility.

(4) Roffo[18] (1936) used white rats, and exposed them to the total sun, or to an ultraviolet lamp of 1,800 to 3,400 angstrom units. He used a Hanau apparatus, the content of ultraviolet being equal to the average of sun units, measured with the dosimeter S. V. He began the exposure to ultraviolet with 5 minutes daily and increased it to 2 hours daily. The longest test lasted 9 months and 5 days.

He started with 10 rats. Three died of insolation.

Of the remaining 7, 3 developed carcinoma of the ears; 3 spindle cell sarcoma of the eye; 2 sarcomas of the ear or neck; all had hyperkeratosis and papillomas of the ears. No controls developed cancer.

(5) Beard[1] *et al.* (1936) exposed white rats to a mercury arc lamp in a pyrex glass globe at a distance of 5 feet, beginning with 5 minute exposure daily, and increasing the exposure to 20 hours daily by the fourteenth day, and continued this dose for about one year. "The pyrex glass globe absorbs most of the ultraviolet radiation shorter than 2,800 angstrom units." Their rats developed carcinomas of the skin of the ears and nose and sarcomas of the eyes. They had never seen spontaneous tumors in their animals.

They say: "The cancer-producing action is believed to depend more on the actinic intensity than on the quantity of rays."

(6) Rusch and Baumann (1939) used inbred strains of mice, with a quartz mercury arc lamp, 50 cm. above the floor of the cage, starting with 10 minute exposure daily and increasing to 30 to 60 minutes daily. They got tumors of the ears of a high percentage of albino mice in 3½ to 9 months. Black mice developed tumors in a much lower percentage and in a longer time.

(C) OUR ANIMAL EXPERIMENTS

We have rayed two groups of a standard strain of white mice, with a quartz mercury arc lamp, the ultraviolet output of which was accurately measured.* One group of mice was rayed 2 minutes daily, at 24 inches; the other group was rayed 2 minutes daily, at 36 inches. Mice of a standard brown strain were included in both groups with the white mice. All mice were on a standard diet, supplemented with bread soaked in irradiated milk.

About one year after beginning the irradiation, some of the white mice began to develop papillomas on their ears, eyelids and backs.

Mouse 1, rayed 2 minutes at 24 inches daily, developed a papilloma of the eyelid of the right eye; this

*The lamp used in all of these studies is a Hanovia quartz mercury arc lamp, model 2210, furnished to me by the Hanovia Chemical and Manufacturing Company. The ultraviolet output of the lamp was checked for me by Dr. Wm. T. Anderson, Jr., of the Hanovia Company, employing a differential type ultraviolet meter calibrated at the National Bureau of Standards, Washington, D. C. The spectral radiation emission from this lamp is characteristic of the unfiltered quartz mercury arc operating at about one atmosphere mercury pressure in the quartz envelope. The total ultraviolet output at 24 in. was 1,130 microwatts per square centimeter (113 erg seconds per square millimeter). The exposure time, distance from the burner, and frequency of irradiation are stated in each set of experiments. The radiation measurements are accurate to about plus or minus 5 per cent, and fluctuations in electrical supply may have resulted in other variations in the radiation intensity amounting in total to a plus or minus 10 per cent.

enlarged and formed an ulcerating fungating lesion involving the region of the right eye. The mouse died after 15 months of irradiation.

The lesion of the region of the right eye was 12 mm. in diameter and extended down into the tissues of the right side of the neck as a mass, 5 x 7 mm., just below the angle of the jaw. The spleen was small; the other organs showed nothing abnormal. Microscopically, the lesion involving the region of the right eye and extending down into the tissues of the right side of the neck is a squamous cell cancer, with marked keratinization and pearl formation (*Figs. 2* and *2a*).

Mouse 2, rayed 2 minutes at 24 inches daily, developed a papilloma on the right ear, which enlarged to form an ulcerating fungating lesion involving the right side of the head, extending to the margin of the eye in front and back to the shoulder. The mouse died after 18 months of irradiation.

The lesion of the right side of the head was 25 mm. long and 17 mm. wide, and extended deep into the tissues of the right side of the neck, toward the angle of the jaw. Microscopically, this lesion involving the right side of the head and extending down into the tissues of the right side of the neck, is a squamous cell cancer, with marked keratinization and pearl formation (*Figs. 3* and *3a*).

In the lower lobe of the right lung of this mouse was a white nodule 7 mm. in diameter; in the upper lobe of the same lung was a white nodule 4 mm. in diameter, and another nodule 1 mm. in diameter. The spleen was very large; the other organs were negative. Microscopically, the nodules in the right lung are squamous cell cancers, in every way like the lesion of the right side of the head (*Figs. 3b* and *3c*).

Mouse 3, rayed 2 minutes at 24 inches daily, did not develop any lesions of the skin; only quite marked inflammation of the margins of the eyelids. This mouse died after 21 months of irradiation; autopsy did not show any lesions of the skin or any lesion causing death.

Mouse 4, rayed 2 minutes at 36 inches daily, developed papillomas on the ears and back; and at the end of 21 months of irradiation it had a large nodule at the base of the right ear, with part of the ear destroyed; and an ulcerating lesion of the posterior margin of the left eyelid. In addition, there was a papilloma on the tip of the left ear and two papillomas on the back, between the shoulders. This mouse died at the end of 22 months of irradiation.

The ulcerating lesion of the eyelid was 10 mm. in diameter and it was rather superficial. Microscopically, it is a simple ulcer, with no evidence of neoplastic change in the epithelium or connective tissue.

Mouse 5, rayed 2 minutes at 36 inches daily, now, with a little over two years of irradiation, has a papilloma on the back between the shoulders, and more recently a small papilloma toward the tip of the right ear. The mouse is in good condition, with no irritation of the eyelids and no change in the cornea.

The brown mice in these two groups did not develop any lesions.

There are no spontaneous tumors of the skin and no spontaneous tumors of the lungs in the strain of white mice used.

(IV) SUNLIGHT, QUARTZ MERCURY ARC RADIATIONS, LIGHT SENSITIZATION, AND LESIONS OF THE SKIN

In any discussion of the action of sunlight, there is very frequently some question of sensitization. Thus, a person who has had a sunstroke is said to be more susceptible to the effects of the sun, and persons who have had a sunstroke say that is true.

An important factor in connection with the action of sunlight is the pigment in the skin and disturbances in pigment production. This is evident in the first part of this discussion, and will be more specifically discussed here.

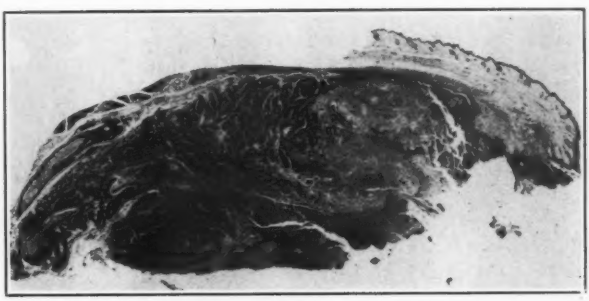


Fig. 2

Mouse 1. Lesion involving the region of the right eye and extending down into the tissues of the right side of the neck. Epidermis above, to the right; extension down into the tissues in the center and to the left (photograph, 16 X).

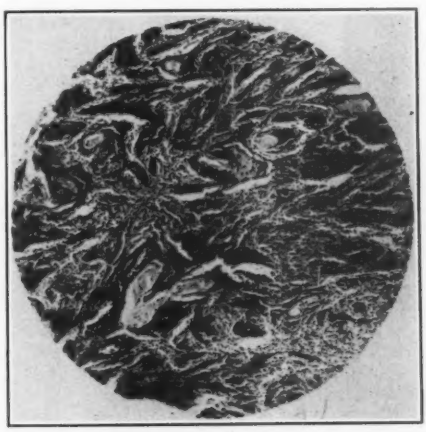


Fig 2a

Photomicrograph of area of infiltration in center of Fig. 2. It is a squamous cell cancer, with marked keratinization and pearl formation (100 X).

A very important factor is the relation of different articles of diet and the action of sunlight on the skin, light sensitizers. Since the skin lesions of pellagra appear especially in the spring, on portions of the skin not covered by clothing, in persons of outdoor occupation, considerable attention was given to the question of a light sensitizing substance; but, with knowledge of the cause of pellagra, such consideration has been dropped. In some parts of this country, there has long been an idea that persons with an outdoor occupation should not eat buckwheat cakes too far into the spring of the year on account of the danger of developing skin lesions. In the same regions there has been the idea that cattle fed on buckwheat in the spring would develop lesions of the skin, especially on the back; and this idea has found its way into the literature, especially with the suggestion of a fungus growing on the buckwheat.

These rather indefinite ideas could be added to by many of you from your knowledge of folk lore. But there are definite clinical observations and animal experiments that can be considered quite carefully.

(A) CLINICAL OBSERVATIONS

In the human, clinical observations refer more to disturbances in pigment production in the skin, indicating something of the complex nature of the production and action of pigment in the skin.

(1) Freckling is one of the simplest disturbances in pigment production in the skin; and the relation of freckling to susceptibility of the skin to untoward effects of sunlight has been considered in the earlier part of this discussion. The pigment in the skin acts as a transformer of radiant energy, and tanning is nature's way of developing protection.* Freckling has been said to be an abortive effort at tanning; and with the present craze for a "sun tan" one sees many pitiful examples of these disturbances in pigment production in the skin.

A young woman, of fairly dark complexion and dark hair, has a white spot in her hair on one side. At 15 years of age she had an attack of catarrhal jaundice (acute toxic necrosis of the liver); and at 19 years of age another such attack. For some years she has had repeated and frequent attacks of urticaria. Superficial injuries leave an unpigmented area of skin, which does not become pigmented, and which burns when she is exposed to the sun. The skin of her hands has lost its pigment to a great extent, as has the skin of her neck; and, when she is exposed to the sun, these unpigmented areas burn, and large freckles form at the border of these areas on the back of her neck and shoulders.

(2) Malignant lentigo is a rare condition in which what appears to be a solitary freckle begins to enlarge, becomes ulcerated, and develops into a squamous cell cancer.

*Painting the skin, especially with the red colors, as of henna, also affords protection.

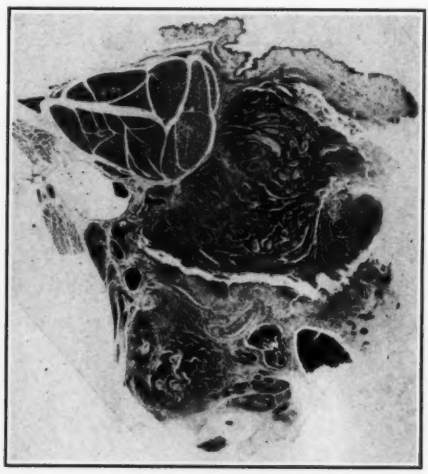


Fig. 3

Mouse 2. Lesion of the right side of the head and extending down into the tissues of the right side of the neck. Epidermis above, toward right; extension down into the tissues beneath the epidermis, extending down to the bottom of the figure toward the right (photograph, 16 X).

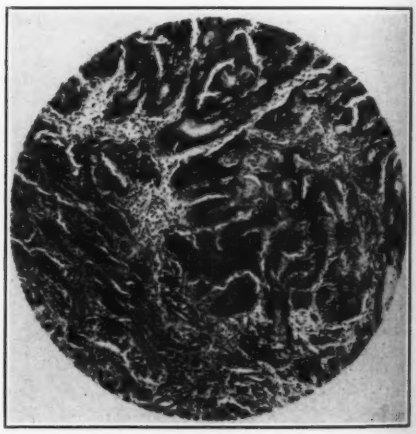


Fig. 3a

Photomicrograph of area of infiltration in center of Fig. 3. It is a squamous cell cancer, with marked keratinization and pearl formation (100 X).

Kob[10] (1922) cites the case of a 74-year-old man: for 30 years he had a small brown fleck in front of the left ear and a larger one on the forehead. During the previous 15 years the small fleck in front of the ear had enlarged, extending in a wavy line toward the nose. Some few weeks before, an ulcer appeared at the site of the original fleck in front of the ear; there was no pain; the ulcer never healed. There was another small fleck above this large patch, over the cheek bone. The area on the forehead remained unchanged. There was a basal cell cancer behind the left ear of 20 years' standing. Microscopic examination of the ulcerated area on the cheek showed the epithelium extending down into the underlying tissue, with pearls, and keratosis on the surface. There were cells loaded with pigment around the area, with an occasional giant cell. There is no indication that this condition has anything to do with light sensitization.

(3) Xeroderma pigmentosum is another rare but interesting skin condition associated with disturbance in pigment formation. Hyde[8] (1906) discussed and figured xeroderma pigmentosum, and said it may be fitly designated as a childhood cancerosis. Beginning commonly about the second year of life, there is a distinct cutaneous hyperemia, followed by a uniform, discrete pigmentation of the exposed parts of the body, with the result of symmetrical freckling of the skin in brownish-tinted macules. As the development of the child proceeds, the freckling is accompanied by much roughness of the surface; there is hyperemia and puffiness of the eyelids; the conjunctivae inflame; there is consequent photophobia; and later, mother-of-pearl-like whitish spots become perceptible between the pigment macules. Minute telangiectatic vessels gradually form in and about the other lesions named, and often small isolated angiomata are scattered among the other oddly associated lesions (*Fig. 4*). Finally, papillomas are formed, almost exclusively over the affected parts; and even at this tender age, epitheliomatous growths develop, classical in type, usually multiple, often of most malignant character.

This chain of morbid phenomena has its genesis in the weakened resistance of the skin of the young child to the more refrangible rays of the solar spectrum; the hyperemia and pigmentation being "simply different endeavors to paralyze the injurious influences of light." "If sufficiently generalized, the melanosis might possibly have secured for the victim of the disease absolute immunity."

"Here, then, we have a true carcinosis of childhood, directly traceable to the action of the more refrangible rays of the solar spectrum, and strictly limited to the exposed parts of the body for its severest manifestations: severest for the reason that the clothing of children especially, and this at the season of the year when the light is chiefly effective, does not offer a perfect barrier to the light."*

(4) Unna[21] (1896) described "carcinoma of the sailor's skin:" the ears, temples and backs of hand and fingers first become mottled and

*Molesworth never saw a case of xeroderma pigmentosum in Australia.

Fig. 3b

Nodule in the lower lobe of the right lung of mouse 2. The nodule is quite sharply circumscribed, with lung tissue above and to the left (photograph, 16 X).

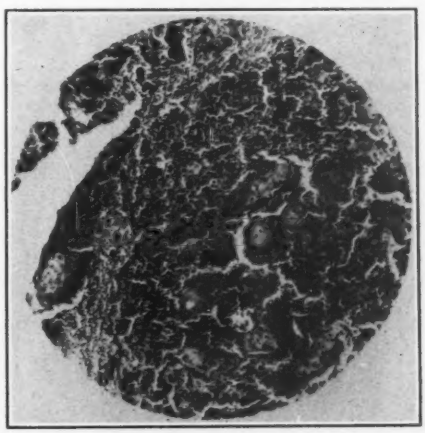


Fig. 3c

Photomicrograph of nodule in lower lobe of right lung. It is a squamous cell cancer, in every way like the lesion of the right side of the head (Fig. 3a). (100 X).

pigmented; later, non-pigmented islands of skin develop between the freckles; thickening, roughening and cornification of the horny layer follow; and eventually the sebaceous glands become hypertrophied and indolent, cancerous growths of the "rodent ulcer" type form.

Fig. 4
Xeroderma pigmentosum, showing pigmentation, telangiectases, atrophic patches, and beginning cancerosis in a child (Hyde).

Fig. 5
Group of three of the author's patients, showing in each lesions of xeroderma pigmentosum; brother and two sisters (Hyde).

Unna says that xeroderma pigmentation so closely resembles the "sailor's skin" that the latter might almost be named "xeroderma pigmentosum of adults." He suggests the operation of the same cause along similar lines in both conditions.

Apparently there is something of a familial character in xeroderma pigmentosum, as Unna speaks of two families, and Hyde figures one (*Fig. 5*). This may be only a family constitution.

When we turn to domestic animals, there is a wealth of reports of light sensitization by the eating of certain plants, usually St. John's wort (plants of the genus Hypericum).

(5) In his practice in southern New Jersey, Rogers[19] (1914) saw an entire herd of Holstein cattle with the white skin hanging in rags, and the dark skin soft and supple as a glove, the condition being due to exposure to sunlight after eating this herb (St. John's wort).

(6) Ray[16] (1914) said that in Tunis and Asia Minor this plant (St. John's wort) poisons goats, cattle and horses; that the effects are manifested only in full light, and only in animals devoid of pigment or with a very lightly pigmented skin. The Arabs protect the skin of the animals with solutions of tobacco or henna; the red tint of the henna is especially good protection. He says the fluorescent red pigment in the plant is the cause of the skin lesions in animals. The essential oil does not cause the skin lesions; this causes the nervous symptoms and death.

(7) Dodd[2] (1920) reported that in Australia the eating of St. John's wort causes dermatitis and itching of the skin in cattle and sheep: horses are not so much affected, and only on white patches of skin. The skin is sensitized, pigmented skin as well as non-pigmented skin, but the pigment in the skin prevents the action of the sun's rays. If the white skin is stained or colored, it is not affected by the sun, even though the animal is sensitized. In a red cow, patched with white, only the white areas were affected. The sensitizing principle is most abundant in the flowers and flowering stems.

(8) Drabble (1929) studied skin cancer in cattle in Australia.

"Brand cancer" is the name applied to any lesion following branding, and is often applied to lesions of the skin not associated with branding. Some of the cases are epitheliomatous. The condition is rare: he found 190 cases in 955,798 head of cattle killed and inspected. Unpigmented portions of the skin were involved in 137 cases (72.1 per cent). These lesions are due to sensitization of the unpigmented skin to the action of the sun's rays as a result of eating light-sensitizing plants by the animal. St. John's wort is the most important plant; and others, as trefoil, also play a part.

(B) ANIMAL EXPERIMENTATION

The studies initiated by von Tappeiner[22] on the light sensitizing action of certain fluorescent substances, and by Hausmann[6] on the light sensitizing action of hematoporphyrin, while of fundamental importance in the study of light sensitizing substances, and of photodynamic activity, do not come within the scope of our discussion.

(9) Rogers[19] (1914) made fluid extracts of certain species of Hypericum (St. John's wort) from New Jersey, and found that 0.1 c. c. of those fluid extracts would kill a 250-gram guinea pig.

(10) Dodd (1920) fed St. John's wort to sheep and reproduced the same symptoms and lesions as occur following the eating of the plant naturally.

(11) Henry[7] (1922) repeated Dodd's feeding experiments, using cattle and sheep (using younger plants than did Dodd), and got the same symptoms and lesions as after eating the plant in nature. He kept cattle and sheep in a pasture of St. John's wort, muzzled so they could not eat the plant. Some of these animals were recovering from the symptoms and lesions produced by eating the plant. None of these animals developed any symptoms or lesions; so he concluded that contact does not produce any symptoms or lesions in cattle and sheep.

(12) Marsh and Clawson[12] (1930) fed cattle and sheep on St. John's wort (*Hypericum perforatum*) from northern California. While rather large feedings were toxic to some of the sheep, none of the sheep died. The plant was much more toxic for cattle, and one animal died. The results were variable; and, while slight dermatitis was produced in a few animals, it was not at all comparable with that described in the literature.

(13) Inman[9] (1939) fed buckwheat flour to guinea pigs for ten days, and one of these pigs exposed to the sunlight died in a few hours.

(C) OUR ANIMAL EXPERIMENTS

As several species of Hypericum grow in the United States, and several in the District of Columbia, we have undertaken a study of the effect of some of these species, with special reference to lesions of the skin, using standard strains of mice, fed on a standard diet, plus bread soaked in irradiated milk.

First Set of Experiments.—As Rogers' fluid extract killed 250-gram guinea pigs in doses of 0.1 c. c., we made 10 per cent tinctures of our hypericum species (our mice weighed just about one-tenth as much as did Rogers' guinea pigs) and injected it subcutaneously. Our first tinctures were: *H. scouleri,* leaves; *H. scouleri,* flowers; *H. perforatum,* leaves; *H. denticulatum,* leaves; and *H. anagalloides,* leaves.

Groups of a standard strain of white mice and of a standard strain of brown mice were given 0.1 c. c. of the tincture subcutaneously daily and then exposed to the sun. The alcohol in the tinctures had a definite but temporary effect on the mice; so, after 16 daily injections of the tinctures, we put the material in the tinctures into cotton seed oil and continued the injections as before (shaking the bottle briskly before taking out the material for injection). These mice were now exposed to the quartz mercury arc lamp, 4 minutes at 36 inches, and then placed in the open sun for one-half hour. The injection, irradiation and exposure to the sun were continued daily: the exposure to the sun was gradually increased to where they were exposed for 2 hours on and after the forty-ninth treatment. The mice became very much excited and jumped in the jar like corn in a popper when they were exposed to the irradiation, especially the sun. When the experiment had been in progress for 3½ months, and the weather had become cold enough so that the mice were exposed in front of a closed window in the laboratory, it was decided to increase the length of exposure to the sun. At the end of two hours' exposure all mice were in good condition; and at the end of three and one-half hours all mice were dead (browns as well as whites).

Second Set of Experiments.—Nine mice were treated as in the previous experiment, but without exposure to the quartz mercury arc lamp; that is, they were given injections of the oil suspension of the Hypericum extracts and were exposed to sunlight. The sun exposure was made regularly in the laboratory, in front of a closed window (it was now too cold to put the mice outside or to have the window open). On the twenty-first day, with a sun exposure of six hours, 7 of the 9 mice were dead (browns as well as whites).

Third Set of Experiments.—Two groups of white mice, a and b.

(a) A group of 12 mice were exposed to the quartz mercury arc lamp, 4 minutes at 36 inches, daily. One mouse died after 10 weeks of irradiation, with no indication that the death was due to the irradiation.

After 3 months of irradiation as above, buckwheat was added to the diet in the form of a buckwheat cake daily, in place of the bread, soaked in irradiated milk. They ate it readily. After 3½ months of buckwheat in the form of cakes, the buckwheat flour was mixed to a paste with irradiated milk and fed to the mice (on the possibility that baking the cakes would destroy the active principle); and the mice are being continued on this, with irradiation as from the beginning.

(b) A group of 12 mice were injected weekly with 0.1 ml. *H. denticulatum* extract in oil; and exposed to the quartz mercury arc lamp 4 minutes at 36 inches daily. Seven of these mice were dead by the end of 10 weeks. Three of the remaining mice developed a marked dermatitis of the entire length of the tail; and in some of them the end of the tail became gangrenous and fell off.* Under continued injection and raying, the dermatitis of the tail cleared up in all mice. This group is being continued, with injection and irradiation, as from the beginning.

SUMMARY

(1) There is ample clinical evidence of the part played by sunlight in the production of lesions of the skin, especially in Argentina and Australia. Persons with very fair skin, and persons with red or sandy hair who freckle, are especially affected. Persons with dark skin, and those who tan readily, are not affected. The lesions are keratosis, basal cell cancer (rodent ulcer type), and squamous cell cancer.

(2) Several workers, using quartz mercury arc lamps, have produced papillomas and carcinomas of the skin, and sarcomas of the eye, in mice and rats.

(3) Using carefully measured doses of radiation from a quartz mercury arc lamp, we have produced papillomas and squamous cell cancer (acanthoma) of the skin in a standard strain of white mice, with metastases in the lung in one case.

(4) Disturbances of pigment formation in the skin, and the action of light sensitizing substances, have long been considered to play a part in the production of lesions of the skin; and there is ample clinical evidence of such relationship.

(5) Plants of the genus Hypericum (St. John's wort) have long had the reputation of being light sensitizers; and several workers have produced dermatitis in domestic animals by feeding the plant.

(6) Using extracts of several species of Hypericum, with sunlight and carefully measured doses of radiation from a quartz mercury arc lamp, we have undertaken to study the production of skin lesions in standard strains of mice. We have used buckwheat in the same way.

(7) We have carefully checked the ultraviolet output of our lamp, the exposure time, distance and frequency, using standard strains of mice on a standard diet.*

(8) The work is being continued, and no conclusions are drawn.

REFERENCES

1. Beard, H. H.; Boggess, T. S.; and von Haam, E.: Experimental Production of Malignant Tumors in the Albino Rat by Means of Ultraviolet Rays. Amer. Jour. Cancer, **27**: 257, 1936.
2. Dodd, S.: St. John's Wort and Its Effects on Livestock. Agric. Gaz., N. S. Wales, **31**:265, 1920.
3. Drabble, T.: Skin Cancer in Cattle. Australian Vet. Jour., **5**:71, 1929.
4. Findlay, G. M.: Ultraviolet Light and Skin Cancer. The Lancet, **11**:1070 (Nov. 24) 1928.
5. Findlay, G. M.: Cutaneous Papillomata in the Rat Following Exposure to Ultraviolet. The Lancet, **1**:1229 (June 7) 1930.
6. Hausmann, W.: Uber die sensibilisierende Wirkung des Hamatoporphyrins. Strahlentherapie, **3**:112, 1913.
7. Henry, M.: Feeding and Contact Experiments with St. John's Wort. Agric. Gaz., N. S. Wales, **33**:205, 1922.
8. Hyde, J. N.: On the Influence of Light in the Production of Cancer of the Skin. Amer. Jour. Med. Sci., **131**:1 (Jan.) 1906.
9. Inman, O. L.: Buckwheat Found a Factor in Light Sensitivity of Skin: Chlorophyll Part of Riddle. Newsweek, p. 27, April 24, 1939.
10. Kob, G.: Ueber Lentigo Maligna, eine seltene, besondere Form des Hautcarcinoms. Beitrage z. klin. Chirurgie, **127**: 709, 1922.
11. Lawrence, H.: The Relative Low Humidity of the Atmosphere and Much Sunshine as Causal Factor for the Great Prevalence of Skin Cancer in Australia. Med. Jour. of Australia, **11**:403 (Sept. 29) 1928.
(The Proceedings of the International Congress on Dermatology, Rome, 1912, were not available.)
12. Marsh, C. D.; and Clawson, A. B.: Toxic Effects of St. John's Wort (*Hypericum perforatum*) on Cattle and Sheep. U. S. Dept. of Agric., Technical Bulletin No. 202 (Sept.) 1930.
13. Molesworth, E. H.: Rodent Ulcer. Suppl. to Med. Jour. of Australia (June 18) 1927.
14. Phillips, Chas.: Skin Cancer in Southwest United States. Third International Cancer Congress, Atlantic City, N. J., Sept. 11, 1939.
15. Putschar, W.; and Holtz, F.: Erzeugung von Hautkrebsen bei Ratten durch langdauerende Ultravioletbestrahlung. Ztschr. f. Krebsforschung, **33**:219 (Dec. 22) 1930.
16. Ray, G.: Note sur les effets toxiques de millepertuis a feuilles crispees (*Hypericum crispum*). Soc. Cent. Med. Vet., **68**: 39, 1914 (1914-1915).
17. Roffo, A. H.: Cancer y Sol. Bull. Inst. Exper. Med., p. 907. Buenos Aires, 1928.
18. Roffo, A. H.: Role of Ultraviolet Rays in the Development of Cancer Provoked by the Sun. The Lancet, **1**:472 (Feb. 26) 1936.
19. Rogers, T. B.: On the Action of St. John's Wort as a Sensitizing Agent for Non-pigmented Skin. Amer. Vet. Rev., **46**: 145, 1914.
20. Rusch, H. P.; and Baumann, C. A.: Tumor Production in Mice with Ultraviolet Irradiation. Amer. Jour. Cancer, **35**:55 (Jan.) 1939.
21. Unna, P. G.: The Histopathology of Diseases of the Skin, p. 724, 1896.

*This is not a very uncommon occurrence in our mice under irradiation with the quartz mercury arc lamp.

*Now, 21 months after the beginning of the experiments, the ultraviolet output of the lamp at 24 inches is 1,040 microwatts per square centimeter (104 erg seconds per square millimeter).

Also, at the present time, our lamp produces a definite but mild erythema on my forearm in 2 minutes at 24 inches; almost the same in 4 minutes at 36 inches; and the merest trace, if any, in 2 minutes at 36 inches.

22. von Tappeiner, H.: Die photodynamische Erscheinung (Sensibilisierung durch fluoreszierende Stoffe). Ergebn. d. Physiol., **8**:698, 1909.
23. Whitmore, Eugene R.: The Biologic Action of Radiant Energy. I. Ultraviolet. Physical Therapeutics, **47**:419 (Aug.) 1929.
24. Woodruff, Chas. E.: The Effects of Tropical Light on White Men. Rebman, 1905.

DISCUSSION (*Abstract*)

Dr. Wright Clarkson, Petersburg, Va.—I happen to live in the southern part of Virginia, and there we have an unusually large number of skin cancers. Dr. Bloodgood was in my town many years ago and I held a clinic for him while he was there. We had 100 or more current cases of skin epitheliomas. Dr. Bloodgood was very much amazed at seeing so many of them at this clinic. I do not know why we have so many cases of skin cancer in Virginia. It is extremely interesting to learn through Colonel Whitmore and other research workers something about the cause of these superficial epitheliomas.

We find, of course, as Colonel Whitmore has said, that we practically never see skin cancer in the negro. I recall only one case, a full-blooded African, with a squamous cell epithelioma on the side of his heel.

We have had several cases where the pigment distribution was greatly altered. Just before I left home I saw a very dark negro girl who suddenly noticed that her hands were getting white, and then her face began to get white in spots. By the time she came to me, only about six weeks later, she was almost a white woman, in so far as her face and hands were concerned.

Colonel Whitmore calls our attention to the well-known fact that squamous cell epitheliomas occurring frequently on the hands, lower lip and ears, metastasize and cause death, while those about the eyes and cheeks are usually of the basal cell type and are not prone to metastasize. We have almost stopped doing biopsies on skin epitheliomas in certain locations because we are frequently able to state that they are not dangerous from their general appearance and location.

We want to find out, in working this problem out with Colonel Whitmore, whether or not we can produce the same effects with roentgen rays and with the gamma rays of radium.

You all know, of course, that many of the pioneers in radiology have died with squamous cell epithelioma of the skin. We know, therefore, that it is possible to produce cancer of the skin in man by small doses of x-ray. It will be interesting to know whether we can do the same thing in mice with x-ray and with gamma ray.

Dr. George T. Caldwell, Dallas, Tex.—I want to call attention to the fact that given a certain susceptibility or hereditary background for the production of cancer, evidently there are several different groups of inciting agents which are capable of starting the growth of cells.

All of us, in the last few years, have been very much interested in the various chemical compounds which are known to cause cancer in experimental animals, with a good deal of clinical evidence that they do so also in human beings. One interesting thing in regard to these is that apparently the inflammatory reaction is not an essential part of the stimulus which leads to cancer production. Aside from the numerous chemical agents that are known to incite tumor growth, apparently there is this well-known group of radiations.

The first x-ray cancer developed within about five years of the beginning of the use of x-ray as a diagnostic procedure, and as recently as last week I still saw an x-ray cancer in one of the early x-ray workers, indicating that it takes a long period of time, at least in some individuals, for radiations of that type to produce cancer.

I want to emphasize, too, that Dr. Whitmore's emphasis on ultraviolet rays is one which is now pretty well recognized everywhere, although his method of producing tumors by this means is of course most fascinating.

Apparently, the various types of radiation constitute a second important group among the incitants of cancer. What we should like to know, of course, is whether these radiations incite cell growth and malignant change directly, or whether they produce some chemical change which then becomes the stimulating or inciting factor.

I suppose we shall have to recognize that there is probably still a third group of incitants to tumor growth, in that there is some indication that even mechanical injuries may be sufficient in some individuals to start the proliferation which ultimately becomes malignant. I am wondering, of course, if that will account for the rather frequent development of osteogenic sarcomas in young persons during the growing period of life, especially, and principally, in those bones that are subject to the greatest amount of trauma during the growth period. Of course, if mechanical traumas of this type incite tumor growth, there must be a susceptibility to tumor growth of such degree that only the relatively slight traumas or injuries of ordinary life may be the starting factor, when combined with the growth stimulus.

I have no doubt that there are other groups of incitants to tumor growth than these three, and the search for additional factors is certainly one of the most fertile lines along which tumor research can go at the present time.

I should like immensely to know what part photosensitization has in the production of tumors, and ultimately, also, what part fluorescence plays in tumor production.

Dr. Whitmore (closing).—Dr. Caldwell spoke of groups in cancer due to chemicals. We do not find anything of groups, apparently, in our mice. All mice, in all three strains we used, are very susceptible to the action of the chemicals we used. As I said, we started using these chemicals primarily to see if our mice were all susceptible to them. We get lesions very quickly, and we have never had mice that did not develop papillomas, some of them in enormous numbers, on the skin. Most of them died before they got carcinoma. Of course, the mouse is a very susceptible animal; but it seems that here we are dealing with uniform susceptibility.

Dr. Caldwell mentioned Dr. Bloodgood's statement that one never saw skin cancer in a beautiful woman. All of them are beautiful! It is a question of protection of the skin. The Australian workers pointed out that one does not see cancer of the skin in women who protect their skin by cosmetics; but they did find cancer of the skin of women who are exposed out of doors. As to whether the chemicals and radiant energy initiate

cell growth or chemical changes, that is your question, Dr. Caldwell, and it is up to you to answer it. I will not try to.

As to the question of trauma in osteogenic sarcoma, one of our members studied the question of osteogenic sarcoma in football players particularly. He considered that those young men would get trauma that might cause osteogenic sarcoma; and he found that such trauma had nothing to do with the development of osteogenic sarcoma.

Dr. Caldwell spoke of photosensitization in cancer. As I said, to date we have no indication that photosensitization causes any more skin trouble than does the straight lamp; but that is a matter for a future report. We do not know now.

STONES OF RECUMBENCY*

By HJALMAR E. CARLSON, M.D.
and
NELSE F. OCKERBLAD, M.D.
Kansas City, Missouri

There are many patients who require prolonged immobilization in bed for one illness or another. A majority of these are orthopedic cases and include such diseases as osteomyelitis, fractures of the pelvis, femur or spine, tuberculous diseases of the spine or hip or poliomyelitis. Other cases may be medical, and include diseases such as arthritis, pulmonary tuberculosis, cardiac or renal conditions. Many of these patients have foci of infection which may contribute to the incidence of urinary tract infection. That recumbency itself might be a factor in the formation of urinary calculi can easily be understood, since the role of stasis and infection in the formation of urinary stone has long been known. That stone may form without the presence of obvious infection is also recognized, and has led to a division of urinary calculi into the stones of the aseptic, primary type and stones of the infectious type, sometimes termed "secondary stone." Just how large a part recumbency may play in the formation of urinary calculi may be of considerable general interest.

Orthopedists have for a long time recognized that urinary stones can form in patients who are subjected to long periods of immobilization, and these surgeons have taken measures for its prevention and treatment. For this reason the urologist seldom sees such cases.

We have had occasion to study eight cases which may be classed as stones of recumbency. The various reasons for recumbency included the following diseases: osteomyelitis, gonorrheal arthritis, pulmonary tuberculosis, posterior poliomyelitic paralysis, angina pectoris, mercury nephrosis and two urological operative cases.

MECHANISM

The processes by which the formation of urinary stones, in prolonged states of recumbent inactivity, are facilitated merits our consideration. From a study of various experimental methods used to produce urinary calculi and from obvious clinical observations the following factors may be considered contributory in promoting the formation of urinary calculi in recumbent patients:

(1) Stasis as a result of continued recumbency.
(2) Decalcification of the bones with increased urinary calcium excretion.
  (a) Localized decalcification of bone near the site of injury or infection.
  (b) Generalized decalcification as a result of immobilization.
(3) Heliotherapy producing (a) increased calcium absorption, and (b) dehydration, by excessive evaporation producing an increased concentration of calcium salts in the urine.
(4) Dietary deficiencies or excesses:
  (a) Excessive calcium intake.
  (b) Excessive alkaline ash diet.
(5) Vitamin deficiencies and excesses:
  (a) Vitamin A deficiency.
  (b) Excess of vitamin D.
(6) Urinary tract infection.
(7) Extra-urinary infections.

(1) *Stasis.*—The importance of stasis as an etiologic factor in the formation of urinary calculi is well recognized. The occurrence of renal stone in cases with obstruction at the ureteropelvic junction is not uncommon and is due to the urinary stasis of the resultant hydronephrosis. When a patient is kept completely immobilized for long periods of time, urinary stasis is also favored. Since urine is a supersaturated solution in regard to the stone-forming salts, it can be readily understood that precipitation may occur when a patient is kept in one position for a long time. It is interesting to note that urine is only a supersaturated solution in regard to its stone-forming salts. All other constituents

*Read in Section on Urology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

are held in a state of simple chemical solution. The stone-forming salts are held in solution by the action of the colloids, and it is generally now accepted that the colloids act by adsorption, which is simply a question of electric potential. Therefore, the apparent solubility of the stone-forming salts is increased. Since the urinary colloids are in a fine state of subdivision, their total surface area is tremendous. However, colloidal suspensions are rarely stable because on standing the particles tend to coalesce and reduce the surface area. We, therefore, find that crystals will form in stale urine. In a recumbent patient we have conditions favorable for the precipitation of stone-forming salts, since the constant bed rest is most favorable for urinary stasis. After the "nucleus" has been formed it is then a question of laying down of salt crystals together with a foreign type of colloid which is probably derived from the serous exudate caused by the irritation or the excoriation of the stone.[1] According to Alexander Randall,[2] the nucleus originally takes the form of a plaque on the papilla in one of the minor calyces. In active patients this plaque is most generally located in the papilla of the lower calyx, since the lower calyx favors stasis, but in the recumbent patient, according to Joly,[1] all calyces are affected equally.

(2) *Decalcification.*—The gradual rarefaction of a broken or diseased extremity as seen on repeated x-ray examinations is well known to all of us, and is probably best seen in fractures of the femur. A disappearance of the contour or stress lines is first observed and following this there is a loss of density of the entire bone. If, however, some movement is permitted, or if physiotherapy is administered, we know that there is much less rarefaction. The effect of recumbency on bone decalcification has been well summarized by Pyrah and Fowweather,[4] who based their conclusions on experiments of Grieg,[3] who in turn showed that hyperemia of the bone produced rarefaction, decalcification and osteoporosis. Pyrah and Fowweather concluded that decalcification is due, therefore, to a relative hyperemia of the bony skeleton. In the active healthy individual a certain balance of blood supply is maintained between the bony skeleton and the muscles and viscera. In the recumbent individual in whom muscular activity is greatly diminished, there is extensive atrophy of the muscles and a diminution in their blood supply. As a result there is a hyperemia of the bone, since more blood is being carried to the bone through the nutrient vessels.

In the recumbent patient we may not only have decalcification of the diseased extremity, but a decalcification of the entire skeleton. A great deal of the calcium which is taken up by the blood serum is excreted by the kidneys, although some of the excess appears in the feces. Observations on the blood calcium after prolonged recumbency have been made by Mawson,[5] who showed that the figure for serum calcium in 34 children ranged between 11.7 and 25.0 milligrams per 100 cubic centimeters. This would at least serve to indicate that blood calcium studies should be done on patients who are kept recumbent for considerable periods. If we add more calcium to a stagnant urine which is already supersaturated in regard to its stone-forming salts, it is small wonder that stones occur in recumbent patients.

(3) *Heliotherapy.*—Recumbent patients are at present subjected to intense heliotherapy. This is true especially in orthopedic and tubercular hospitals where heliotherapy almost appears to be a religious rite. A consideration of the effect of heliotherapy is, therefore, quite important, since it has been shown by many that an excess of vitamin D will produce an increased absorption of calcium from the bowel and a high serum calcium. Whether or not the sun's rays will produce sufficient synthesis of vitamin D by the skin is open to some question. There is no doubt that it is produced, but it is generally regarded, as shown by Harris,[6] that pigmentation of the skin produces a natural defense of the body against the overproduction of vitamin D by the sun's rays. The studies of Mawson suggested that heliotherapy may be a factor in the formation of urinary calculi while other studies by Pyrah and Fowweather minimize the effect of heliotherapy and the latter believe that the pigmentation of the skin is a sufficient defense against hypervitaminosis D resulting from the action of the sun's rays. However, we wish to call attention to the fact that there is a considerable number of white people who apparently have very little protection against the sun's rays, as evidenced by repeated blistering, redness or freckling instead of a regular tan which is at present generally regarded as the typical and desired protective and decorative coating.

The effect of heliotherapy in increasing the evaporation of water from the skin with a resultant concentration of the urine has also been

studied by Pulvertaft.[7] A study of the specific gravity of the urine of 23 patients for a period of twelve months receiving routine sun treatment showed the average monthly specific gravity to be constant (1.018) and showed no difference between winter and summer months. On the other hand, Hoyle[8] suggested that prolonged exposure to the sun in tropical climates may be a cause of stone in the kidney. In certain areas of hottest tropical Africa the natives void only once in 24 to 48 hours. In our own community, there was a definite increase in the relative number of stone cases seen during the drought years of 1932 to 1937 with its attendant high temperatures. We are, therefore, of the opinion that recumbent patients subjected to heliotherapy should have an adequate supply of fresh palatable water to compensate for both the noticeable and insensible perspiration that occurs. Unless the patient drinks large quantities of fluid there is no doubt that the urine will be much more concentrated than normal with an increased tendency for salts to be thrown out of solution. If in addition calcium is being excreted by the kidneys as a result of decalcification of the skeleton the precipitation, especially in regard to the calcium salts, will be increased.

(4) *Vitamin Deficiencies and Excesses.*—(a) Vitamin D: a few remarks in regard to the effect of an excess of vitamin D have already been made under a consideration of heliotherapy. A great many experiments in animals have been made using excessive amounts of vitamin D either in the form of ergosterol or other forms of the vitamin. We have all heard of observations in human beings where excessive administration of vitamin D not only as ergosterol but also as cod liver oil have resulted in renal calcification as well as calcification in other portions of the body. According to Harris,[6] the optimum therapeutic dose does not seem to be far removed from the toxic overdose, and it is, therefore, advisable to adhere closely to the correct dosage. That some recumbent patients may have an idiosyncrasy to vitamin D, as do some ambulatory individuals, must be taken in consideration and the development of toxic effects appreciated. These toxic effects include vomiting, blood in the urine and hypercalcemia with gradual failing health.

(b) *Vitamin A Deficiency.*—During the past few years an increasing number of experiments have shown the importance of an adequate intake of vitamin A in preventing the formation of stones in experimental animals. The calculi which result in animals from a deficiency of vitamin A consist for the most part of calcium phosphate. In regard to human observations it is quite well known that calculi are particularly frequent in areas where the diet is deficient in vitamin A. However, in hospitals there is generally an adequate intake of vitamin A, since vegetables are on the menu daily. In addition, many children's hospitals administer additional vitamin A, which is contained in cod liver oil. We, therefore, should not expect a vitamin A deficiency to occur, although, if such a deficiency were present the formation of calcium stones would be enhanced.

(5) *Dietary Deficiencies and Excesses.*—(a) High calcium diet: in some hospitals large quantities of milk are served, particularly to children. Generally, most of the calcium is excreted in feces in normal patients, as shown by Cantarow.[9] In recumbent patients we have seen above that a great deal of the calcium is excreted in the urine. Whether the same is true for the calcium contained in foods is open for consideration.

(b) *Acid versus Alkaline Ash Diets.*—We know that certain foods, namely, meat, fish and cereals, will produce an acid urine while other foods such as vegetables and certain fruits will produce an alkaline urine. In the past few years a great deal of attention has been paid to the control of the reaction of the urine by means of diet, mainly for the prevention of more stones after operation, but in some instances it is advocated for the purpose of causing the disappearance of calculi already existent. In stones of recumbency, as we have seen, the stones are almost all calcium stones. This would then indicate the need for an acid ash diet. In an alkaline urine both dicalcium and tricalcium phosphate are precipitated. If the urine is kept strongly acid the calcium phosphates are kept in solution as the soluble monocalcium salt. While we hesitate to say that an acid ash diet will cause the disappearance of firm calculi, it does seem reasonable to expect that soft putty-like masses of calcareous debris will disappear. Certainly an acid ash diet is indicated in the prevention of stones of recumbency where an increased calcium excretion occurs.

(6) *Urinary Tract Infections.*—That calculi can occur without obvious urinary tract infection is well known, but that clumps of infected material may act as a nucleus for the formation of a calculus is also recognized. The presence

of infected material can also serve as a cement substance to further the enlargement of the stone. Recumbent patients have a higher incidence of urinary tract infection and would, therefore, be more likely to have a higher incidence of urinary calculi. This is true particularly in patients with injuries or diseases of the spine where nerve injury occurs with a resultant paralysis of the ureter and bladder. It is well nigh impossible to keep interns from catheterizing a distended cord bladder despite standing rules to the contrary. Ascending infections in these cases then become the rule.

(7) *Extra-urinary Tract Infections.*—Much experimental work has been done showing that focal sepsis may be associated with renal calculi. In fact, Alexander Randall says that all calculi result from the presence of infection. In many recumbent patients the infection is the cause of the patient's being recumbent. Such extra-urinary tract infections include secondarily infected fractures, osteomyelitis, Pott's disease, gonorrheal or other arthritis or tuberculosis with secondary infection.

INCIDENCE

Although many patients remain recumbent for long periods of time without the development of any renal calculi, the incidence of calculi in recumbent patients is definitely higher than in normal individuals. In 150 war cases with fracture of the femur, Wilson,[10] in England, reported that 23, or 15 per cent, had renal colic and hematuria. Key[11] reported urinary tract complications in 19.1 per cent of 162 recumbent children. The important factor apparently in producing calculi in recumbent patients is the degree of recumbency to which the patient is subjected. Ninety-seven per cent of the children observed by Key were immobilized in dorsal decubitus for an average of 97 weeks. However, stones did occur in three children who had been immobilized only 7.8 and 13 weeks, respectively.

In 60 cases collected by Pulvertaft, 27 per cent of the stones vanished without surgery by tilting the bed. The stones were still present in 30 per cent and were removed surgically in 9 per cent. Armstrong[12] reported that for two and one-half years he had been turning the patients 4 to 10 hours every two weeks and that he no longer had urinary tract complications.

TYPES OF STONES IN RECUMBENCY

As might be expected, stones of recumbency are generally calcium stones. Even in children the majority are calcium stones. Key analyzed the stones in children and found that only 15 per cent were uric acid or ammonium urate.

The stones of recumbency differ from the general type of stones, since most calculi of non-recumbent patients consist of uric acid or ammonium urate. Of 644 renal calculi collected at Brooklyn, the calculi were found to be of the following types:[13]

472 were uric acid or ammonium urate or the small yellow to brown, very smooth or very rough variety.

78 were magnesium ammonium phosphate (with a little calcium phosphate or oxalate) or the grayish-white type of calculus of variable sizes and shapes.

88 were calcium oxalate (12 contained some carbonate) or the small brown to black stone which is rough.

4 cystin.

1 fibrin.

1 xanthin.

0 indigo.

0 urostealith.

The shape of the stones of recumbency is of two distinct types. Either the calculi are round or oval or they are the branching type which begins first in the calyces and eventually forms a cast of the entire renal pelvis. The first type is generally more firm, has the same general appearance as the stones usually seen, and must be removed surgically. The second type is often soft and generally disappears spontaneously when a patient is allowed up and about (*Fig. 1*).

SYMPTOMS AND DIAGNOSIS

The symptoms are the same as those seen with calculi in non-recumbent patients, that is, colic, blood in the urine and often the passage of the calculus in a few days. Sometimes the attack of colic occurs while the patient is still recumbent, but more typically it occurs when his position is changed after being recumbent for a long period of time. This corresponds to the onset of renal colic in non-recumbent patients who often develop renal colic following exertion such as that which may occur on the early days of their summer vacation. The diagnosis is substantiated by x-ray examination. Since most of the stones are calcium stones, even the earliest calculi can be seen on a good x-ray plate.

CASE REPORTS

We present below eight cases which we think can properly be classed as stones of recumbency:

Case 1.—H. S., a white man, aged 19 years, was first seen in the hospital in the spring of 1933 with an osteomyelitis of the right hip and right clavicle and a large pelvic abscess. He gave a history of having had osteomyelitis for three years, which followed the lancing of a small abscess over the eye and was followed by high fever and signs of generalized septicemia. The blood cultures showed a pure culture of *Staphylococcus aureus* at the onset. He had spent most of the past three years in bed. The hip had been drained several times. A subtrochanteric osteotomy was done once and on at least two occasions he had been in a spica cast for three months. He had no symptoms referable to the urinary tract, although the urine had contained considerable pus and some albumin since the onset of his illness.

On x-ray examination of the hip in 1933, an irregular calculus was seen in the right kidney lying in the lower calyx which was 2 by 1 centimeter in size. A review of the previous x-ray plates taken in 1930, 1931 and 1932 did not show the presence of any calculus. Because of the patient's generally poor condition, the stone was not removed. Further x-ray studies made in 1937 and 1938 showed no change in the size of the stone. The urine in 1938 was free of pus and was negative for albumin. When last seen he had no intentions of having the stone removed. He had little apparent disability from his osteotomy, and he was living with a woman who had kept him supplied with life's necessities.

Case 2.—M. W., a white woman, aged 19 years, was first seen in the spring of 1933 with generalized gonorrheal arthritis of two years' duration. At the onset of the disease in 1931 she was in bed for three months and in the spring of 1932 she was in bed again for three months following manipulation of the hips and knees and the application of a spica cast. The end result was excellent.

When she was seen in 1933 she complained of pain over the left kidney with radiation over the crest of the left ilium. The urine was entirely negative. Cystoscopy and pyelographic examination showed a stone in the lower calyx and a larger stone at the ureteropelvic junction. The stone in the pelvis was removed by pyelotomy and the stone in the calyx by nephrotomy. She has had no further trouble.

Case 3.—E. M., a white woman, aged 28 years, was first seen in the fall of 1933. She had been in bed constantly for the previous three years because of pulmonary tuberculosis with cavity formation. At the time she was seen she complained of intermittent pain over the right kidney, radiating downward above the crest of the ilium, of two years' duration. She knew that she had had a stone for the preceding two years, and that the urine contained pus and albumin and that no tubercle bacilli had been found. Six months prior to admission to the hospital some hematuria was observed. The pain was more severe and the patient complained of dysuria. The patient said that her menstrual period was four days overdue. A pregnancy test done, using a Wistar

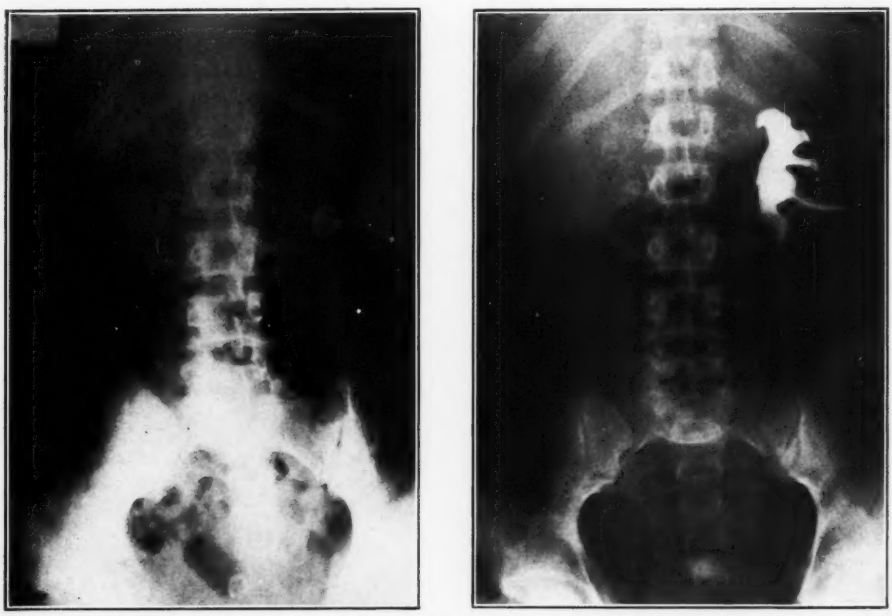


Fig. 1
X-ray showing formation of calculi in recumbent patient and disappearance when ambulatory.

albino rat, was found to be positive. Cystoscopic and pyelographic examination showed a calculus in the right renal pelvis 2 by 2 centimeters. This was removed by pyelotomy.

Nine months later she was delivered of a baby boy. Four years after the pyelotomy she again had pain in the right renal area. She stated that in the intervening period she had been free of pain, but that she knew that she must have another kidney stone. She said that during the previous four years she had had adequate rest, but no continuous bed rest until the previous year when she had been in a sanitarium on strict bed rest. Cystoscopic and pyelographic examination revealed another calculus with considerable pyonephrosis present. This time a nephrectomy was performed.

Case 4.—L. H., a white man, aged 31 years, was first seen in the summer of 1937 because of persistent large amounts of pus in the urine. Cystoscopic and pyelographic examination showed the presence of a large calculus in the left kidney with a pyonephrosis of 20 cubic centimeters. A pyelolithotomy was done. Following the operation there was considerable purulent drainage and healing of the wound was delayed. Ten days after operation a large indwelling ureteral catheter was introduced to try to facilitate healing. X-ray examination was negative. The catheter was removed. After four weeks in bed, ureteral catheterization was again done, which showed an obstruction at the ureteropelvic junction which, on x-ray examination, was seen to be due to a stone. Because of the marked renal damage found at operation, a nephrectomy was done.

Case 5.—J. B., a white man, aged 22 years, was first seen in the fall of 1938 complaining of a dull aching pain over the left kidney, which he said he had had as long as he could remember. The pain was never very severe and disturbed him most on his frequent fishing or hunting trips. Cystoscopic and pyelographic examination showed an infected hydronephrosis of 40 cubic centimeters due to an aberrant renal vessel. At operation the vessel was found and was divided and ligated. A nephrostomy was done. About three weeks following the operation, when the patient was ready to get up, he complained of moderately severe pain over the other kidney. An x ray plate showed the presence of calcareous material in the untreated kidney which partially filled all of the major and minor calyces. The patient was nevertheless allowed up and about and a week later an x-ray examination showed that the calcareous material had disappeared.

Case 6.—P. H., a white woman, aged 23 years, was admitted to the hospital in the summer of 1939. She had been in bed for a major portion of a year following an attack of generalized poliomyelitis. Part of the time had been spent in a respirator. When she was seen in 1939 she presented a residual paralysis of the entire left side of the body from the shoulder downward as well as a residual paralysis of the right leg. She complained of pain in the right back and right lower quadrant with dysuria for a period of three months prior to her urological admission. The urine showed 2,500 pus cells per cubic millimeter on microscopic examination and albumin was one plus.

Cystoscopic and pyelographic examination showed a large staghorn calculus in the right kidney with a considerable degree of pyonephrosis present. Due to the patient's generally poor condition, operation was deferred.

Case 7.—W. B., a white man, aged 56 years, was admitted to the hospital in the summer of 1939 and was kept on bed rest for six weeks because of angina pectoris. On admission, he also complained of intermittent attacks of pain over the right kidney region and right lower quadrant with radiation into the penis and inner aspect of the right thigh for four months prior to his admission to the hospital. Twelve years previously he had a similar attack and passed a large calculus. On his present admission, cystoscopy and pyelography showed a calculus in the right ureter one centimeter from the ureterovesical orifice. Several unsuccessful attempts were made to remove the stone transurethrally and finally the stone was passed from the ureter by the patient. We extracted it from the terminal urethra.

Four weeks after his admission to the hospital he began to have pain over the left kidney with radiation over the crest of the ilium. Cystoscopic and pyelographic examination showed that calculi had formed on the left side while he was in the hospital. These passed spontaneously and he has had no further urinary complaints since he left the hospital.

Case 8.—B. C., a white man, aged 38 years, was first seen in the summer of 1939. He had been in bed for a period of three months with severe nephrosis, and he had been comatose or semicomatose at intervals, at times for a week or more. Evidently the nephrosis was the result of mercury injections given sixteen years previously for lues because of severe toxic reactions that occurred at that time and the undoubtedly severe renal damage. The urine on admission to the hospital showed four plus albumin and a few pus cells. A kidney-ureter-bladder plate showed the presence of very large kidneys on both sides and the presence of a small calculus in the lower calyx on the left side. An x-ray examination made three months prior to his present hospital admission by his physician did not show any opacities. The stone had formed in the interval.

PROPHYLAXIS

Since something is understood concerning the factors favoring the formation of stones of recumbency, the formation of such calculi may be guarded against. The following prophylactic measures can therefore be taken:

(1) *Change of Position.*—If we are to believe the results of Pulvertaft and Armstrong that even infrequent and minimal change in position will prevent the formation of stones of recumbency or even the disappearance of existing calculi then this procedure occupies first place in the prophylaxis of stones of recumbency. According to Pulvertaft, 27 per cent of the stones disappeared without surgery by tilting the bed, and according to Armstrong the turning of the patient for 4 to 10 hours every two weeks was sufficient to prevent urinary tract complications. It seems advisable to put the patient on the best type of frame or cast available for a reg-

ular change in position rather than to allow him to remain in the same position for long periods of time.

(2) *Adequate Fluid Intake.*—A large quantity of palatable water should be available for the patient at all times to prevent concentration of the urine. Nurses should realize that it is not sufficient to see that palatable water is kept on the stand by the patient's bed, but that they should also see that he gets the water. Many recumbent patients cannot reach the water and often are reluctant to bother anyone. The greater the exposure to heat the larger will be the fluid loss, and, therefore, the larger the fluid intake necessary. Fruit juices should not be given, as they produce an alkaline ash and an alkaline urine.

(3) *Acid Ash Diet.*—It is not necessary to produce a highly acid urine, but it is advisable to keep the urine on the acid side so as to keep calcium in solution. Of all the diets devised, an acid ash diet contains about as many palatable foods as any diet could contain. These foods include all fish and meats, as much milk, butter, cream or eggs as desired and bread and cereals of all kinds. Food to be avoided are mainly fruits and vegetables, but there are many of these also permitted. In institutions where many recumbents are cared for the control of diet is easy, but in isolated instances additional attention is necessary.

(4) *Cod Liver Oil.*—The use of cod liver oil is advisable particularly in children, both for vitamin A and vitamin D, for the reason that its vitamin A content is an aid in preventing the formation of calculi.

(5) *Physiotherapy.*—It is difficult to institute physiotherapy on many recumbent patients, but some decalcification of bone can be prevented by routine daily massage and active movement of limbs which are not splinted. There will be more blood to the soft tissues of the parts, and therefore less rapid decalcification of the bone itself.

(6) *Adequate but not Excessive Heliotherapy.*—A certain amount of heliotherapy is advisable to maintain muscle tone and circulation. Excessive heliotherapy is to be avoided because of the dehydration produced and the possible synthesis of excessive vitamin D by the skin, especially in patients lacking in so-called normal pigment response to the sun's rays. It is wise to avoid exposure to the sun during the middle of the day when these processes will be at a maximum.

(7) *Control of Urinary Tract Infection.*—We have evolved a simple rule for the control of urinary tract infection which consists in administration of sulfanilamide when the pH of the urine is under 6.0 and the administration of mandelic acid when the pH is over 6.0. If we do not find that there is an immediate disappearance of the infection, cultures are made to determine the infecting organism. If the urinary infection occurs in an acid urine, then most certainly sulfanilamide is indicated. We have found that small doses of sulfanilamide, such as five grains three times a day, are sufficient to control most urinary infections. We, therefore, obviate the danger of producing a nucleus of sulfanilamide or acetylsulfanilamide on which a calculus can form. That calculi can form in this way with the larger doses of sulfanilamide and other related substances is now well recognized. If, on the other hand, the infected urine is alkaline, mandelic acid generally fortified with ammonium chloride is used. In general, it is not considered advisable to extend the acid ash features of the diet to approach that of the ketogenic diet because of the objectionable nausea and other digestive disturbances which frequently follow.

TREATMENT

If the recumbent patient has had an attack of ureteral colic with or without the demonstration of blood in the urine, or if he has had blood in the urine without ureteral colic, it is advisable to adopt all the prophylactic measures described above even though no shadow is seen on the x-ray plate. Certainly if we have the symptoms of ureteral colic in a recumbent patient we may assume that conglomerate calcium masses have formed. If microscopic examination of the urine reveals the presence of pus, urinary antiseptics should by all means be administered.

If x-ray examination reveals the presence of calculi which appear to be poorly defined, as is shown in *Fig. 1*, it is also wise to follow the same plan of treatment, since it has been shown that calculi of this type will invariably disappear if proper measures are taken.

If, on the other hand, more firm rounded calculi are found on x-ray examination which are generally regarded as being too large to pass through the ureter, it is safe to assume that these

calculi will eventually have to be operated upon. No harm will be done in trying the measures outlined until the patient's general condition is such that operation can be considered. Certainly such treatment may prevent the calculus from becoming larger, although it may not cause its entire disappearance.

If the calculus is highly obstructive or if a severe grade of pyonephrosis is present, the urological problem then becomes of first importance.

SUMMARY

(1) Stones occur more commonly in recumbent patients than in normal individuals because recumbency itself favors urinary stasis. Other etiologic factors include excessive urinary calcium from decalcification of the skeleton, dehydration from inadequate fluid intake often as a result of intense heliotherapy, inadequate vitamin A intake, particularly in isolated recumbent patients, excessive vitamin D intake, excessive calcium or a high alkaline ash diet, the presence of urinary tract infection, especially with cord bladder, and the presence of extra-urinary foci of infection.

(2) Stones of recumbency are most frequently calcium stones, and so differ from stones in non-recumbent patients which generally consist of uric acid or urates. Their shape is variable and can be either round or ovoid or they may partly or entirely fill the calyces with a gritty, putty-like type of material which solidifies with prolonged recumbency.

(3) The symptoms are those of kidney colic and most generally occur with a change in a patient's position after a period of prolonged recumbency. Generally at least seven weeks of strict recumbency are necessary to produce stones, although some cases are reported in a shorter time.

(4) Adequate prophylactic measures taken in the case of recumbent patients will generally prevent the formation of renal calculi. Most important is a change in the patient's position, although other measures such as adequate fluid intake, physiotherapy, cod liver oil, acid ash diet, adequate but not excessive heliotherapy, and the control of urinary tract infections with proper medication are of distinct value.

(5) When calculi have formed or the symptoms of renal colic occur even though calculi cannot be demonstrated, the institution of the prophylactic measures outlined will cause a disappearance of symptoms. The gritty, putty-like type of calculus, even though visible on x-ray examination, will also disappear. Similar treatment in the case of firmer calculi will not cause their disappearance, but may prevent their enlargement. If the calculus is highly obstructive, or severe pyonephrosis is present, surgical interference is necessary.

(6) Eight cases with stone of recumbency are presented. Of these, one patient showed a spontaneous disappearance of stones from the kidney when he was allowed to get up and one patient passed his calculi. Three were removed surgically and three were not operated upon. Of those not operated upon, one refused operation, one had a marked residual post-poliomyelitic paralysis, and one had a severe nephrosis.

REFERENCES

1. Joly, J. S.: The Etiology of Stone. Jour. Urol., **32**:541, 1934.
2. Randall, A.; Eiman, J. E.; and Leberman, P. R.: Studies on the Pathology of the Renal Papilla: Relationship to Renal Calculus. J.A.M.A., **109**:1698, 1937.
3. Grieg, D. M.: Clinical Observations on the Surgical Pathology of Bone. Edinburgh: Oliver & Boyd, 1937.
4. Pyrah, L. N.; and Fowweather, F. S.: Urinary Calculi Developing in Recumbent Patients. Brit. Jour. Surg., **26**:98, 1938.
5. Mawson, E. E.: A Consideration of Some Possible Factors Concerned in the Development of Urolithiasis in Children. Liverpool Med. Chir. Jour., **7**:99, 1932.
6. Harris, L. J.; and Innes, J. R. M.: Mode of Action of Vitamin D: Studies on Hypervitaminosis D; Influence of Calcium-phosphorus Intake. Biochem. Jour., **25**:367, 1931.
7. Pulvertaft, R. G.: Nephrolithiasis Occurring in Recumbency. Jour. Bone & Joint Surg., **21**:559, 1939.
8. Hoyle, J. C.: Biochem. Jour., **23**:457, 1931, quoted from Pyrah and Fowweather.
9. Cantarow, A.: Calcium Metabolism and Calcium Therapy, 2nd Edition, p. 31. London: H. Kimpton, 1933.
10. Wilson, W. E.: Renal Colic and Hematuria Following Recumbency. Brit. Med. Jour., **2**:101, 1931.
11. Key, L. A.: Urinary Tract Complications in the Prolonged Immobilization in Children. Brit. Med. Jour., **1**:1150, 1936.
12. Armstrong, A. C.: Urinary Tract Complications in Prolonged Immobilization. Brit. Med. Jour., **1**:1274, 1936.
13. Kamlet, J.: Analysis of Renal Calculi. Jour. Lab. & Clin. Med., **23**:321, 1937.

DISCUSSION (*Abstract*)

Symposium on Urinary Calculus, papers of Dr. Wm. M. Coppridge, Drs. Alfred I. Folsom and Harold A. O'Brien, and Drs. Hjalmar E. Carlson and Nelse F. Ockerblad. Paper of Dr. Coppridge was published in the January issue, page 18; and paper of Drs. Folsom and O'Brien in May, page 455.

Dr. Linwood D. Keyser, Roanoke, Va.—I wish to deal chiefly with the etiology of stone, following the lead of Dr. Randall. His demonstration of the morphogenesis of primary calculus and its development on the renal papilla make many features of the pathology of stone better understood.

The physicochemical features of calculus formation entail the simultaneous precipitation of crystalline matter with the gelling of urinary colloids, this intimate concomitant precipitation resulting in a colloid-crystalloid aggregate. Such aggregates undergo secondary in-

ternal molecular readjustment and compaction, the colloid organic matter becoming the cementing material of the dense stone.

Animal experimentation in the artificial production of stone approaches the problem from another point of view than that of morphogeny. By causing an extensive hyperexcretion of crystalloid in the animal's urine, calculi are formed. This has been accomplished with oxamide, calcium oxalate and calcium carbonate.

In hyperexcretion calculosis produced by oxamide and calcium oxalate, we found the renal collecting tubules clogged with crystals, this phenomenon suggesting the second type of renal papilla lesion which Dr. Randall has described. Yet these calculi in the experimental animal seldom seemed to be actually attached macroscopically or microscopically to the renal tissue. Furthermore, the urinary sediment always contained an abundance of atypical coalescent crystals showing all degrees of calculous growth in the urinary stream. Stones found at autopsy lay free in the calices, in the pelvis, ureters or bladder.

In hyperparathyroidism we see at least one of the clinical confirmations of such a hyperexcretory mechanism where more calcium salts are excreted than the urinary colloids, salts and hydrotrophic substances can keep in solution or in a state of isolated units on precipitation at a given hydrogen ion concentration.

Yet as Braasch and others have pointed out, we have an excessive calcium excretion in the urine in hyperthyroid disease. Here stone is not increased in incidence. Why this difference from hyperparathyroid urinary hyperexcretion? Is some toxic effect on the urinary epithelium active in one condition and not in the other? Is a chemical or bacterial toxic irritation necessary to form calculus in hyperexcretory states?

An experiment which is suggestive is demonstrated with the slide. The right kidney of a rabbit exposed through a lumbar incision was transfixed from cortex to medulla with a steel needle and the electrocoagulating current momentarily applied. The kidney was replaced and the incision closed. An alkaline diet containing about 0.5 gram of powdered calcium carbonate was given daily. After three weeks of this slight hyperexcretion a small calculus was found at the site of the traumatic coagulation in the renal papillary region. No stone or sand was found elsewhere.

This experiment suggests the possibility of stone formation at a site of the renal trauma, which may be toxic, ischemic, bacterial, or even traumatic.

In addition to experimental hyperexcretory calculosis, stones in animals starved on vitamin A and those produced by inoculation of urea splitting bacteria from stone forming patients come up for consideration. The stones of vitamin A deficiency may have an origin in the renal papilla, but according to Grossman's study they seem to arise at different areas of the urinary tract from encrustation of keratotic epithelium with the calcium carbonate of a highly alkaline urine.

A study of secondary infectious calculi has led to certain conclusions. Trauma to the urinary epithelium seems to localize the infectious process in the bladder or kidney pelvis. Engrafted upon such an area the urea-splitting organisms grow and spread directly causing a lime salt deposition upon inflamed or necrotic epithelium. Such encrustations break away to form stone. I have demonstrated the growth of such secondary calculosis in the human kidney and in experimental animals. This subject has been dealt with in previous reports.

I wish today to present experimental evidence which demonstrates beyond doubt the specific action of urea-splitting organisms in producing stone. A patient with a persistent proteus infection and recurrent renal and ureteral stones provided the organism. A few drops of a fresh culture was injected with a hypodermic syringe into the pelvis of the right kidney, the latter being exposed by lumbar incision. The animal was sacrificed after six weeks. The autopsy picture is striking. The entire right urinary tract is the site of extensive encrustation and calculosis. The right half of the bladder shows radial areas of encrustation extending from the right meatus. This encrustation extends to the midline of the bladder where it suddenly ceases.

The left half of the bladder is clear, as are the left ureter and the left kidney. The cultures from the right kidney revealed, of course, the proteus. Those from the left kidney were sterile.

The clinical association of urinary lithiasis with urea-splitting organisms is noteworthy. Chute, from the Massachusetts General Hospital, found about two-thirds of their recurrent stones due to the proteus. Mayo Clinic observers note a lower incidence. Dr. Coppridge reports an unusually high incidence of staphylococci in his series. This reminds us of the high incidence of staphylococci found in stone by continental European observers such as Hellstrom, Hryntshak and Rovsing. The urologist must endeavor to isolate bacteria and determine their type. Also, we must, I believe, use one of the appropriate culture media to determine the urea-splitting properties of bacteria associated with stone, a point our Chairman has well emphasized.

With regard to proposed solvents for stone, when I presented a case in 1933 in which urinary acidification was successful, I little realized what a variety of procedures would be suggested in the six years that have passed. Personally, I believe that what we may be able to dissolve are the early crystalloid colloid aggregates which I mentioned as the precursor of true stone. This same patient, with whose proteus I produced the unilateral calculosis shown a few minutes ago, passes frequently such slimy mucoid-crystalline matter in all degrees of density. These soft aggregates quickly dissolve upon reduction of his proteus infection with sulfanilamide and then acidifying the urine. What do not disappear are two compact dense stones in the right kidney which slowly grow from year to year and which will soon present the problem of another operative removal.

Using a continuous irrigation apparatus to bathe freshly removed calcium phosphate stones we have found that they are, if dense, most resistant to acids, citrates, metaphosphates, phosphates, urea, magnesium salts, and, in fact, every chemical thus far suggested. True, the surface softens, but soon this is enclosed in a colloidal film which protects the calculus from further chemical action. For these reasons I am frank to admit that I am discouraged in the effort to dissolve true dense calculi of any composition with present methods of diets, drugs, direct irrigations and the like.

Stone is a surgical problem, and it is chiefly in the prevention of recurrence that our efforts may be fruitful. Clear up stone surgically, establish drainage, reduce local and focal infection to the minimum, fight

down especially urea-splitting organisms, and correct the calcium, phosphorus and uric acid metabolism. These are our chief weapons in fighting against recurrence. With zealous effort on the part of urologist and patient, a reasonable amount of luck, and the ability to take a great deal of disappointment, such present methods will help us until something more specific comes along.

Drs. Folsom and O'Brien have presented a splendid survey of bilateral calculus disease. Their discussion of air pyelography and of the stasis produced by stenosis of the caliceal infundibulum are features worthy of emphasis.

The stone of recumbency, so well discussed by Dr. Carlson, is another enigmatic feature of urolithiasis. Vitamin deficiency, infection and perhaps most frequently a dyscrasia of the calcium phosphorus metabolism are presented as etiologic hypotheses, each at present lacking sufficient evidence for scientific acceptance. The prevention and therapy of such stones have been dealt with sufficiently to warrant no elaborative discussion on my part.

Dr. Thomas D. Moore, Memphis, Tenn.—Dr. Randall's brilliant researches on stone formation have struck at the taproot of the problem and he has presented convincing evidence that nephrolithiasis is often the manifestation of a constitutional factor as indicated by the intratubular deposit of calcium in the renal papillae, to be followed by the development of a stone at this site. The conception that renal lithiasis is a disease must now be changed to the newer conception that it is a symptom and that in removing a stone, symptomatic treatment is being instituted and that the job has not been finished until the disease which caused the stone to form has been identified and eradicated if possible. Only then has the urologist's duty to the patient been fulfilled.

At this point I should like to direct attention to the necessity of being constantly on the alert for the recognition of hypercalcemia secondary to hyperparathyroidism. Unless urologists are ever mindful of this disease, many cases will go unrecognized. In a recent case of a proven parathyroid adenoma a true stone had not formed but there were extensive pericaliceal deposits of calcium which illustrate very nicely Dr. Randall's conception of Type II calcinosis. In this case the blood calcium estimation was 18 mg. per one hundred c.c. and the blood serum phosphorus 2.9 mg. During the next four days postoperatively the estimations of blood calcium were 17, 15, 12, and 10 mg. respectively. Follow-up roentgenograms in this case have disclosed no evidence of extension of the calcification but that the deposits seem to be permanent. In another instance of proven parathyroid adenoma, stones had repeatedly formed over a six-year period. Bilateral nephrolithiasis was present requiring surgical treatment; chemical analysis of the stones revealed almost pure calcium phosphate. The blood calcium estimation was 17.1 mg. and the blood serum phosphorus 2.5 mg. These values returned to normal four days following removal of the parathyroid adenoma.

Dr. Coppridge has presented a very reasonable and conservative estimate of the problem of ureteral stones. It is noted that there is an absence of the enthusiastic effort to remove all ureteral stones by manipulative means and that the percentage of those cases treated by open operation is somewhat higher than in other published reports. This may be construed as evidence of conservatism. It will be generally agreed that his ideas of promoting adequate drainage and combating infection in many cases are of more importance than removal of the stone. In my experience, however, the use of the McKay stone dislodger has yielded prompter results in the removal of ureteral stones and has been attended by less inconvenience to the patient than the employment of multiple catheters.

Time forbids a full discussion of the paper of Drs. Folsom and O'Brien. The remarkable recuperative ability of the so-called functionless calculous pyonephrosis as mentioned by Dr. Folsom coincides with my own experience. In an instance of a typical pyonephrosis, 63 c.c. of thick pus was aspirated; the catheter was left *in situ* following which the urine soon became remarkably clear, attended by a rapid return of function. Pelviolithotomy and a temporary nephrostomy were performed. Pyelograms repeated six weeks later revealed an essentially normal kidney and the function was only slightly impaired.

Dr. Carlson's paper on stones of recumbency should be read or heard by orthopedic surgeons, neurosurgeons, and others dealing with cases requiring long periods of recumbent confinement. No doubt those of us who have been privileged to hear his report will adopt the measures he has suggested in the management of these cases with especial reference to prophylaxis.

Dr. Jefferson C. Pennington, Nashville, Tenn.—I shall not attempt to discuss the papers but shall bring up one or two problems which have been foremost in my mind.

My first problem deals with the time of formation of stones and the growth of stone. I have a picture of a stone which was proven by repeated pictures to have stayed in a particular situation in the left ureter for seven years without change in size. Finally this man consented to removal of that stone, which we did by abdominal approach. That condition in the kidney, in spite of drainage, did not improve much.

A year later, this patient formed a stone in the right ureter, invisible to x-ray, which we removed by manipulation. Two years later the same patient was seen with the right kidney filled with stones and the condition of the left kidney, not much improved. The culture in this case was *Proteus vulgaris*.

The other problem I wanted to mention is the relation stones have to families, if any. I operated also on the father of this patient for stones and I have in my list of patients four brothers and sisters all of whom we have operated upon for stones, and some of them three or four times.

A woman went to a surgeon complaining of back pain. He decided that she had something wrong with her uterus and did a hysterectomy, after which carcinoma of the body of the uterus was found. During her stay in the hospital she had to be catheterized frequently, and after she left the hospital she had a marked frequency and was sent to us on account of the frequency, with the presumption that the catheterization in the hospital, from which she had been away for a month, had caused her trouble. And when we x-rayed her we found both kidneys filled with stones. We have no idea how long the process of formation was.

We saw a man, one of two brothers upon whom we operated, both for stone. Both the patients' kidneys are now full of stones.

Six weeks after removal of stones from the right kidney we took another x-ray and found two rather large stones in the right kidney. We presumed that these stones were not removed at the time of operation. Then for the second time we got the stones and reconstructed them according to the x-ray picture and found that they fitted the picture exactly. Then we wondered if stones were coming back in that length of time.

Six months after that picture was made we took another x-ray picture and found that the right kidney had again filled with stones. The culture all along in his urine was both *Staphylococcus aureus* and *Staphylococcus albus*.

While listening to Dr. Carlson's paper on recumbency I remembered the frequency of kidney stones in cases of fracture of the spine, and in some of these cases we have found blood clots as a nucleus of the stone. For a while we did not consider recumbency the principal cause, but probably it had its part also. Also I thought of the Tuberculosis Hospital in Nashville, which has, I think about 150 patients. The patients are all bedridden because the hospital is too small and they avoid taking ambulatory patients if possible. They take only the worst patients. Most of these patients are completely bedridden. In visitations to this hospital over a period of thirteen years we have seen only one kidney stone, and therefore we wonder why these people do not have kidney stones from recumbency.

Some mention was made of heliotherapy as a possible contributing cause of stones. The tuberculous patients just mentioned had massive doses of heliotherapy for months at a time.

Dr. Henry J. Lindner, New Orleans, La.—Aside from controlling of the infection that exists in the kidney in calculous disease, also the eradication of other foci of infection, and regulation of diet, nothing is of more importance in the prevention of recurrence than thorough lavage of the kidney with sterile water following the removal of the calculus and the use of the nephrotomy tube for a week or ten days.

Dr. Jarratt P. Robertson, Birmingham, Ala.—A few years ago I removed a stone about three centimeters in size from a patient's left ureter, three inches from the kidney pelvis. About ten or twelve days following the removal of the stone, the x-ray showed that stones had formed in both kidney pelves. During the next two and one-half years this patient underwent five operations for the removal of renal calculi. One kidney was operated upon three times, the other kidney twice. X-rays from forty-eight to seventy-two hours following each operation failed to reveal calculi, but in only one instance was the patient ever able to leave the hospital before the x-rays demonstrated a reformation of stones in the kidney pelvis.

He was studied by Dr. Albright and his associates, who said that he had no evidence of hyperparathyroidism. He had a proteus infection.

Dr. Alexander Randall, Philadelphia, Pa.—We have seen today very graphically outlined the broad concept of the problem of stone. I have tried to present the simplest picture. Naturally we have run into other types, and time has not allowed of any exposition of them.

Dr. Keyser referred to the Type II lesion of the papilla, I having shown you only Type I. Type II occurs in 1.9 per cent of our autopsy series as compared to 19.6 per cent of what you have seen today, which we call Type I.

We have repeated his experiments; we have traumatized experimentally dogs' kidneys; we have seen calcification on the injury. And yet that is not what man has. It was one of the reasons why, in our first autopsy searches, we expected to find trauma. But we did not find it. Therefore, that type of etiology simply does not hold water in our approach to the etiology of stone.

We have also done considerable experimentation and considerable clinical investigation of the problem of avitaminosis. It has been reported that twenty-four out of twenty-five cases of stone were proven by the Jeannes test to be suffering from avitaminosis or hypovitaminosis. When I asked the man who reported that what type of stones they were, he said: "All types of stones."

We have been watching for three years every stone case by means of the Jeannes test. My collaborator stopped me the other day with a bright look in his eye and said: "I found our first case of avitaminosis by that test." I do not know how many stone cases have passed through his hands. It has been going on for three years.

We all know the role of infection. We all know that such crystallization is rapid. We all know that crystallization in the presence of urea-splitting organisms is calcium phosphate only.

Now, after all is said and done, where there is smoke there is bound to be fire, and it is not correct to throw away or throw overboard or discard or pay no attention to serious minded work that has been done along any of these lines.

Let me summarize some of our experimental work for you. We have had 112 rats in thirteen different groups and on eight different forms of avitamin or hypovitamin diet, and we have killed them at lengthening intervals, hoping to get the early pictures. We were not interested in waiting until x-rays showed calculi; we wanted to know what led up to that calculus. We have seen the characteristic aseptic ulceration of the fornix, we have seen the hyperkeratinization of the lining mucous membrane. We have seen calcification in the kidneys. We have seen it always as a tubular calcification, and we have seen it from the tip of the papilla in the glomerulus. It is a generalized renal affection. There is a definite mucous membrane change. There is hypercalcinuria. What more do you want?

But this is not the clinical case we see of primary uric acid or calcium oxalate stone. All those rats had to be pushed to a marked hypovitaminosis and sometimes we had, in trying to go slowly, to give them cod liver oil to keep the experiment running. But it does produce a condition which can produce a stone, and it belongs, I know, to Dr. Keyser's group of hyperexcretory stone formation, and it belongs to what we call our Type II lesion, and there is a general nephritic and pyelitic reaction and it forms in our autopsy series a very small percentage.

We have taken two groups of sixteen dogs each and attempted to reproduce an active, mild hyperparathyroidism. We have sacrificed one kidney at three to

four months for study and carried the dogs along on the second kidney and sacrificed them up to six months. We have produced calcification in tubule walls extending from one end of the kidney tubule to the other; we have had calcification form in the capsules. It, too, is a general nephritic reaction, and essentially is not our Type I lesion.

We have had two dogs, one in each of the groups of sixteen, that have shown us a typical calcium plaque. Now, remember, dogs not infrequently have renal calculi. Nevertheless, these two dogs, and they only, have given us a microscopic picture similar to our human. Again both of these groups of cases, dogs and rats, have been free of infection.

Thirdly, we have been interested in the problem of the large role of infection, recognizing not the secondary infection that comes after stone is grown, but production of stones by infectious methods.

In dealing with this possible causative factor, infection, we have been forced to discard true renal infection and to think in terms of what the toxin does, the toxin that is circulating in the body from a distant focal infection. We have found it very difficult to get a weak toxin and a lot of our early work produced too drastic symptoms, but it produced two things: one, the kidney does excrete toxin; second, in excreting toxin it concentrates toxin, and in our rabbits that concentration runs from two and one-half to sixty-four times the concentration at the same moment in the renal blood supply. The kidney, as you know, tries to concentrate all its excretory products, so it was not unusual to find these two facts. But the one fact which we have seen is that that damage is in the terminal tubule, where concentration stands at its greatest, and there we have seen really drastic tubular damage under this experimental approach.

Frankly, today I think we have to accept hyperparathyroidism. We all know what a small per cent that represents in the clinical run of patients. I think we have to accept also the possibility of hypovitaminosis, realizing again what a small per cent of patients in this country are suffering from hypovitaminosis. Probably the greatest answer to all is further perseverance in trying to relate renal damage to toxin excretion from distant foci. If we keep those three points of view constantly in front of us, we have a fairly logical approach to the question of every patient: "What am I to do, Doctor, to keep from going through this again?"

It has been mentioned, and properly so, that highly dilute urine does not crystallize as readily as highly concentrated urine. It has not been sufficiently accentuated that in addition to that, focal infections of all sorts should be unquestionably gotten rid of.

Dr. Folsom (closing).—I made a point in my paper that did not seem to strike.

Air pyelograms are of value in showing not only questionable shadows, but also calcifications on the papillae in the substance of the kidney. Nothing will quite show them and localize them as does air.

Question—When you are doing an air pyelogram, how do you know that you have enough to make the picture?

Dr. Folsom—The same way that you know that you have enough skiodan, by causing pain. If they have not pain, I continue until they do or until I think they have enough.

Dr. Carlson (closing).—First, in regard to the low incidence of stones of recumbency in hospitals for tuberculosis, most of the patients who are in these hospitals are not strictly recumbent. They may be in bed, but for the most part are allowed some degree of movement. They get up on one elbow or they turn on their side and therefore there is little opportunity for absolute urinary stasis to occur. This would then serve to support the contention that minimal changes in position are sufficient to prevent stones of recumbency.

I am willing to grant Dr. Randall the premise that stones may develop from calcium plaques on the papillae of the minor calyces, but I believe that the other etiologic factors which have been considered in stone formation should not be too hurriedly cast aside. Generally we consider that uric acid and urate stones are the most common but in recumbency almost all of the stones consist of calcium. Some of the other factors must therefore be involved.

THE GRADING OF RECTAL CANCER*

By TOM E. SMITH, M.D.
Dallas, Texas

In 1828, Frederick Salmon,[1] the founder seven years later of St. Mark's Rectal Hospital in London, in his excellently and lucidly written monograph, "Stricture of the Rectum," said:

"Were I to hazard an opinion, I should say that carcinomatous disease of the rectum originates in a peculiar condition of the mucous glands of the part."

Said Herbert Mayo[2] in his treatise, "Injuries and Diseases of the Rectum," in 1833:

"The most formidable disease of the rectum, from its severity, its fatal character, and its frequency, is carcinoma."

Said T. B. Curling,[3] in 1876, in his book, "Diseases of the Rectum":

"Carcinoma may attack any part of the bowel, but generally affects the lower portion within three inches from the anus. It is liable to be developed also, though less frequently, at the point where the sigmoid flexure terminates in the rectum. The disease primarily developed in the intestine is frequently confined to this organ and to adjoining structures, no other part of the body being found after death secondarily affected. But this is not always so. The lymphatic glands in the vicinity of the rectum often become enlarged; the liver is occasionally invaded by tubercles, and the peritoneum also studded with scirrhous deposits, and similar disease may be developed in the lumbar glands, and other internal parts."

These quotations reveal study of the problem

---

*Read in Section on Proctology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

*From the Department of Proctology, Baylor University College of Medicine.

of rectal cancer with remarkable astuteness by these pioneers. However, it is quite clear that information gained up to 1880 concerning rectal cancer dealt only with subjective and local objective findings, treatment and gross pathology as determined macroscopically at autopsy.

Microscopic attention to cancer of the rectum was stimulated in England by Harrison Cripps and in America by W. H. Van Buren about 1880.

Harrison Cripps described the microscopic findings of "cylindrical epithelioma" in his book "Cancer of the Rectum" and emphasizes the mucous membrane follicular hypertrophy and "new adenoid growth" in the submucous tissue which we know to be an infiltrative process (*Fig. 1*).

Van Buren[5] had his friend and colleague, Dr. T. A. Stimpson, make histologic studies of cases they saw together.

"Stimpson recognizes hypertrophy of the Lieberkuhn follicles as the first in a series of morbid changes in cylindrical epithelioma, and this is followed by the development and multiplication of new follicles in their immediate neighborhood in the submucous tissues."

From this simple beginning pathologists and clinicians have carried on by adding their observations and conclusions, and forty years later in 1920, Dr. A. C. Broders[6] of Rochester, Minnesota, recorded an idea regarding grading of malignant neoplasms on the basis of cell differentiation which gave the medical world its first scientific basis for arriving at a prognosis in rectal cancer.

Broders[7 8] later modified his system of grading to the one we know today, and in 1928 in an article with Rankin[9] proved that histologic grading by his method provided an aid to prognosis in 598 cases of rectal carcinoma.

Until Broders gave us our first system of grading rectal cancer there was much confusion in the classification and practically no agreement by proctologic authorities. To illustrate:

Mayo[10] in 1833 classified rectal carcinomas as being of "scirrhous" or "fungoid" types.

Curling[11], in 1876, classified "carcinomatous degeneration" into three forms of "scirrhous," "encephaloid," and "colloid."

Mathews,[12] the father of American proctology, classified rectal carcinoma into "scirrhous or chronic carcinoma," "encephaloid or acute carcinoma," "squamous epithelioma," and "columnar-cell epithelioma" in 1893.

Alfred Cooper, Swinford Edwards, and the Allinghams[13] of London in 1901 divided rectal carcinoma under three heads: "laminar," "tuberous," and "annular."

This confusion in classification has largely been cleared up by Broders, and since 1928 the problem of classifying or grading of rectal cancer has resolved itself down to forming a basis for prognosis and aiding in selecting correct surgical extirpative procedures.

Broders'[8] classification is histologic only and falls into four classes, each class being designated as a "grade." Grade 1 has differentiation ranging from 100 to 75 per cent and undifferentiation from 0 to 25 per cent. Grade 2 has differentiation ranging from 75 to 50 per cent and undifferentiation from 25 to 50 per cent. Grade 3 has differentiation ranging from 50 to 25 per cent and undifferentiation from 50 to 75 per cent, and Grade 4 has differentiation ranging from 25 to 0 per cent and undifferentiation from 75 to 100 per cent.

Because Broders' classification was solely on a histologic basis, Cuthbert Dukes[14] of London in 1932 outlined a new method of grading of rectal cancer founded on the degree or extent of spread which involved the rectal wall and adjacent lymphatics.

Fig. 1

Showing infiltration of submucosa and muscular coat with "new adenoid growth" (adenocarcinoma). (From Harrison Cripp's "Cancer of the Rectum.")

Dukes grades the cancers following surgical removal. If the carcinoma has not spread through the rectal wall he classes it as Group A. If the carcinoma has penetrated the rectal wall but has not invaded the adjacent lymphatics, he terms it Group B. If it has spread through the rectal wall and has invaded the local lymphatics, he designates it Group C (*Fig. 2*).

In 215 cases operated upon, he

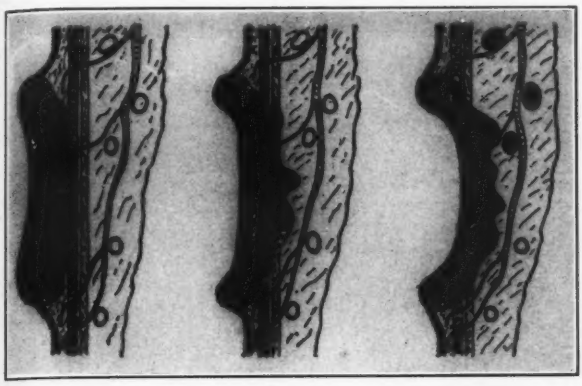


Fig. 2
Showing Group A, B and C from left to right. (Courtesy Cuthbert Dukes.)

found 38, or 18 per cent, to be A cases; 76, or 35 per cent, B cases, and 101, or 47 per cent, C cases.

Among 94 perineal resections he found the 5-year survival rate to be: Group A, 91 per cent (24 cases); Group B, 64 per cent (36 cases); and Group C, 16 per cent (34 cases). Thus Dukes felt that the determination of extent of spread in the surgically removed specimen, and keeping in contact with the patient following discharge from the hospital formed a scientific basis for accurate prognosis for future cases graded by A, B, and C grouping.

Dukes felt that full confidence could not be placed in Broders' preoperative biopsy histologic classification alone because in 20 straight cases he biopsied a fragment and later, after removal, the excised tumor was graded histologically without knowledge of preoperative grading. Dukes found agreement in only four cases (20 per cent), three of which belonged to grade 2 and one to grade 3.

Other observers such as Lockhart-Mummery,[15] Wood and Wilkie,[16] and Bacon[17] agree with Dukes in being unable to base judgment entirely on biopsied tissue and histologic grading. Bacon feels that different portions of the growth vary histologically and quotes McCarthy's findings that different portions and even different areas in the same field show different grades.

Buie[18] in analyzing Dukes' criticism had an associate (Brust) examine 200 biopsy reports before and after surgical resection to determine whether histologic grading from biopsy was accurate preoperatively. In 60 per cent there was complete agreement. Seven per cent showed sections which varied only from grade 1 (high) to grade 2 (low). In 30 per cent there was a difference of one grade only, usually between grades 1 and 2. In 3 per cent there was a difference or error of two grades in two cases and three grades in another. From these results Buie concluded that Broders' method of grading was of preoperative and prognostic value and preferable to Dukes' grading.

Feeling that the study of the lymphatics immediately adjacent to the growth was not quite adequate, Gabriel, Dukes, and Bussey[19] in 1935 advocated formalin fixation of the removed specimen of rectal cancer with dissection of lymph nodes immediately adjacent to the growth and all glands up to the inferior mesenteric vessel ligature.

They felt that microscopic study of all lymph nodes up to the ligature would give additional information toward prognosis and they suggested grouping all C cases into "C 1" and "C 2." "C 1" cases included rectal cancers which had penetrated the rectal wall and invaded the adjacent lymphatics but had no metastic spread involving lymph nodes as far as the inferior mesenteric ligature. "C 2" were those cancer cases involving all lymph nodes even up to the inferior mesenteric vessel ligature or pedicle.

Bussey made a natural sized drawing of the removed specimen and accurately filled in on the drawing the site of dissected and histologically studied lymph nodes. Invaded nodes were "blacked in" while innocent nodes were left "blank." In this fashion the spread of cancer in the perirectal lymphatics was charted. These were called "gland charts" (*Figs. 3* and *4*).

Gabriel, Dukes, and Bussey said that lymphatic spread was upward in the regional vessels along the superior hemorrhoidal vessels to the inferior mesenteric vessel pedicle. They found no cases of the downward or lateral spread of which W. Ernest Miles[20 21] often speaks.

This lymphatic dissection was done in 100 cases and metastasis was found in 62 cases. Cases with only one lymph node involved were found in 13 instances. Cases with two lymph nodes were found 11 times; 3 nodes in 7 cases, and 4 or more in 31 cases.

It is interesting to note that in 1242 lymph

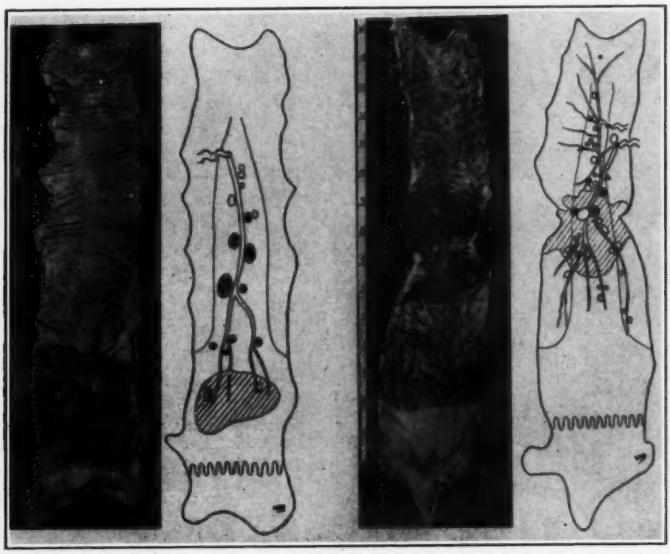


Fig. 3
Shows "gland chart" with metastatic glands "blocked in." Both are "C 1" cases. (Courtesy W. B. Gabriel, Cuthbert Dukes and H. J. R. Bussey.)

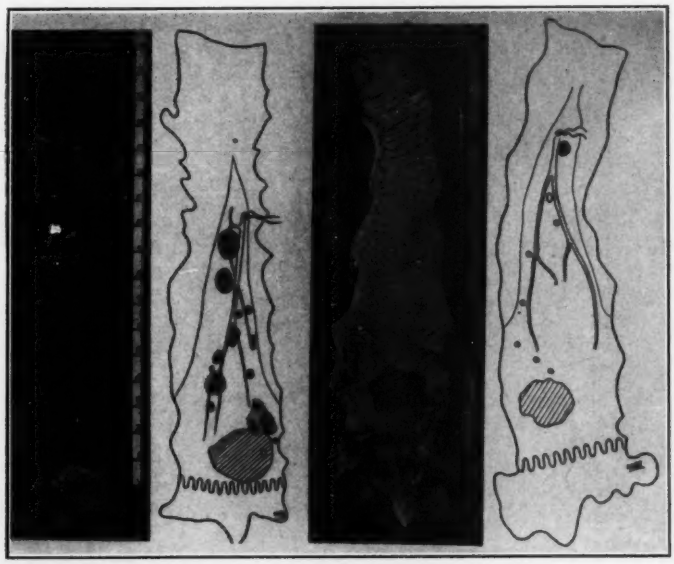


Fig. 4
"Gland Charts" illustrating "C 2" cases. (Courtesy W. B. Gabriel, Cuthbert Dukes and H. J. R. Bussey.)

node dissections there was only a 2 per cent error in nodes diagnosed negative by palpation with finding of metastasis following histologic study and an error of 61 per cent in nodes diagnosed positive for metastasis by palpation with no metastasis found on histologic study.

Concerning lymphatic spread, Gabriel[22] later describes an orderly upward spread of cancer metastasis and says that only one case of "discontinuous lymphatic spread" was found as compared to 6 instances by Wood and Wilkie.[16]

Just as there have been authorities who have criticised Broders' method of grading cancer, there have been others who criticise or ignore Dukes' method of grading. Such authorities as Buie[18] and Yeomans[23] say in their texts that Broders' classification is sufficient to fulfill all requirements regarding selection of method of treatment and prognosis. They neither outline nor advise Dukes' grading system.

The third and last method of grading that will be discussed is that of Wood and Wilkie.[16]

These workers, in an excellent article in the *Edinburgh Medical Journal* in 1933, outlined their method of grading cancer of the rectum, based on the study of 100 cases.

They advise preparing a large section of one-half of the rectum in a longitudinal axis which includes the tumor and rectal wall above the

mass. They further advise smaller sections for microscopic detail.

One of the best clinical descriptions of the "fascia propria" or "sheath of the rectum" ever given is found in their article. They stress the "sheath" as a limiting membrane and say that all the arteries, veins and lymphatics lie in the perirectal fat which is included in this "sheath." They point out a fact of clinical significance, that removal of the rectum includes its lymphatics; therefore, there is no use in attempting to clean out lymph nodes in the hollow of the sacrum at operation, since they are not there (*Fig. 5*).

Fig. 5
Illustrates the "fascia propria" or "sheath of the rectum" with perirectal fat, vessels and lymphatics enclosed. (Courtesy Wood and Wilkie.)

Wood and Wilkie dissected the lymph nodes in this series of 100 cases and found 1,123, or 11.2 per specimen. Forty-nine specimens showed no lymph node metastases, while 51 cases had lymph node involvement.

Their method of grading is a combination of an originally modified Broders' and Dukes' classification.

Broders' classification has been modified to a basis of histologic changes limited to the low power field. Their Grade 1 includes well formed acini lined with differentiated columnar cells. In Grade 2, the acini are markedly irregular and the lining epithelium is more undifferentiated. They describe this as the largest group and most typical adenocarcinoma. Grade 3 includes acini that for the most part have lost their lumina so that they have the appearance of solid cords. Grade 4 is the so-called "colloid" adenocarcinoma typified by malignant hyperplasia of mucous forming elements, with mucus distending the cells to form "signet rings."

After grading the cancer microscopically on the above basis they then study the specimen according to Dukes' method and group it into A, B or C classifications. They term this combination "group grading" (*Fig. 6*).

The following table analyzes their 51 cases with lymph node metastasis:

		Dukes' Grading		
		A	*B*	*C*
Wood-Wilkie Grading	Grade 1, 16 cases....7	7	2	
	Grade 2, 29 cases....	17	12	
	Grade 3, 3 cases....	1	2	
	Grade 4, 3 cases....		3	

Close study of Wood and Wilkie's plan will cause admiration for their scientific work, but it can be readily seen that their method could not be universally adopted, for there would be too great an individual variation by pathologists.

It is interesting to note that within the last two years Dukes[24] has defended histologic grading which he at first criticised on the basis of its inaccuracy and inadequacy.[14] In defending Broders' classification, Dukes takes an admirable stand scientifically, for he says that his own

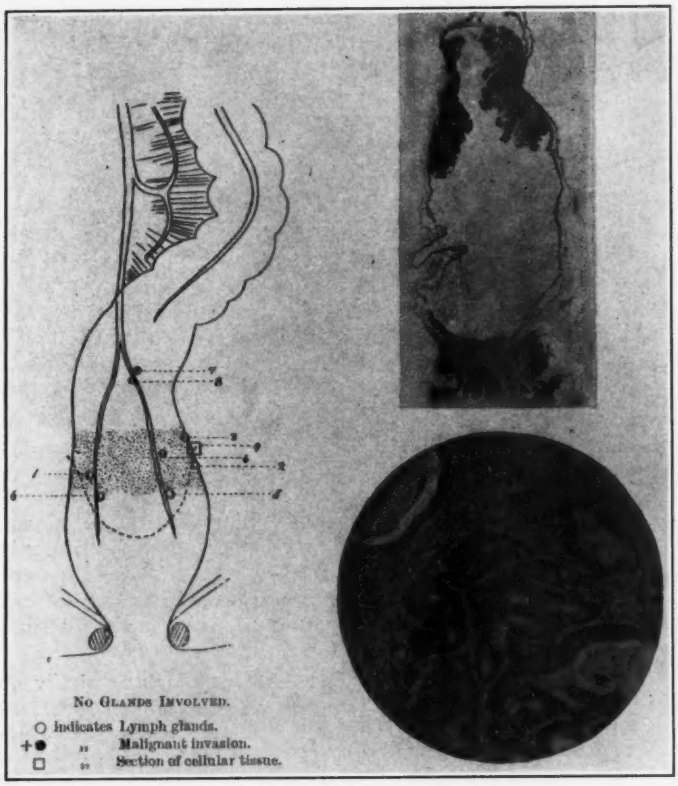


Fig. 6

Illustrates the Wood-Wilkie "group grading." The "gland chart" on the left shows no lymphatic involvement, thus it is grouped as an "A" case. The microscopic section shows it to be Grade 1 Wood-Wilkie modification of Broders' grading. "Group grading" would be Group A, Grade 1.

work with Broders' grading has shown him that "it is a natural and practical method of grading tumours."

In an article published only last month regarding examination and classification of rectal cancer Dukes[25] reports that a combination of Broders' and Dukes' classification is indicated because Broders' grading determines "the rate of growth" and Dukes' grading determines "the extent of spread" which answer two very important questions for the surgeon, namely: (1) How fast is the tumor growing? and (2) How far has it spread?

The purpose of this paper has been two-fold: (1) to discuss the methods of grading of rectal cancer, and (2) to make an appeal for rectal surgeons to have a combination Broders-Dukes grading done by their pathologists in order that in the future more accurate information may aid us in the study of the rectal cancer problem. Rankin and Graham[26] sum up this last purpose beautifully when they say:

"Given the microscopic grading of the degree of malignancy in a case of carcinoma of the colon or rectum and the information as to whether the glands in the specimen were or were not involved by malignant extension, one should be able to estimate with considerable accuracy the ultimate end results."

SUMMARY AND CONCLUSIONS

(1) The high lights of the history and evolution of grading rectal cancer have been listed.

(2) Methods of descriptions of rectal cancer have been briefly sketched.

(3) Methods of grading of rectal cancer have been discussed.

(4) An appeal for the adoption of Dukes' grading to be combined with Broders' grading has been made.

BIBLIOGRAPHY

1. Salmon, Frederick: Strictures of the Rectum, p. 62. James Bullock, 1828.
2. Mayo, Herbert: Injuries and Diseases of the Rectum, p. 188. Burgess and Hill, 1833.
3. Curling, T. B.: Diseases of the Rectum, p. 155. J. & A. Churchill, 1876.
4. Van Buren, W. H.: Diseases of the Rectum, p. 333. H. K. Lewis, 1881.
5. Ibid., p. 330.
6. Broders, A. C.: J.A.M.A., **74**:656, 1920.
7. Broders, A. C.: Minn. Med., **8**:726, 1925.
8. Broders, A. C.: Med. Jour. & Rec., **121**:133, 1925.
9. Rankin, F. W.; and Broders, A. C.: Surg., Gyn. & Obst., **46**:660, 1928.
10. Mayo, Herbert: Injuries and Diseases of the Rectum, pp. 192-194. Burgess & Hill, 1833.
11. Curling, T. B.: Diseases of the Rectum, p. 154. J. & A. Churchill, 1876.
12. Mathews, J. M.: Rectum, Anus and Sigmoid Flexure, p. 374. New York: D. Appleton, 1893.
13. Allingham, W. and H. W.: Diseases of the Rectum, p. 319. Bailliere, Tindall & Cox, 1901.

14. Dukes, C. E.: Jour. Path. & Bact., **35**:323, 1932.
15. Lockhart-Mummery, J. P.: Diseases of the Rectum and Colon, p. 317. Bailliere, Tindall & Cox, 1934.
16. Wood, W. Q.: and Wilkie, D. P. D.: Edinburgh Med. Jour., **40**:321, 1933.
17. Bacon, H. E.: Anus, Rectum and Sigmoid Colon, p. 599. Philadelphia: J. P. Lippincott, 1938.
18. Buie, L. A.: Practical Proctology, p. 378. Philadelphia: W. B. Saunders, 1937.
19. Gabriel, W. B.; Dukes, C. E.; and Bussey, H. J. R.: Brit. Jour. Surg., **23**:395, 1935.
20. Miles, W. E.: Surg., Gyn. & Obst., **52**:350, 1931.
21. Miles, W. E.: Postgraduate Surgery, **1**:1413. New York: Appleton-Century, 1931.
22. Gabriel, W. B.: Principles and Practice of Rectal Surgery, p. 263. W. K. Lewis, 1937.
23. Yeomans, F.: Proctology, p. 519. New York: Appleton-Century, 1936.
24. Dukes, C. E.: Proc. Royal Soc. Med., **30**:25, 1937.
25. Dukes, C. E.: Amer. Jour. Surg., —:181 (Oct.) 1939.
26. Rankin, F. W.: and Graham, A. Stephens: Cancer of the Colon and Rectum, p. 151. Springfield: C. C. Thomas, 1939.

DISCUSSION (*Abstract*)

Dr. Mark M. Marks, Kansas City, Mo.—In 1935 I had the privilege of discussing this problem with both Dr. Dukes and Sir David Wilkie. Both had independently arrived at similar conclusions in regard to gradation of bowel neoplasms. They believed that in malignancies in younger individuals classification was of little importance, since small primary lesions can rapidly metastasize; whereas in older persons, large, fulminating local growths can show little tendency to spread.

On dissecting vessels along with the lymphatics, in the surgical specimens, it was found that vascular invasion occurred more frequently in the younger age groups.

It is my opinion that vascular resistance increases with age, along with the decrease in elasticity.

Dr. T. C. Moss, Memphis, Tenn.—As a clinical pathologist called upon daily to grade tumors, I have always felt acutely the inadequacy of grading according to the classification of Broders. I have given the classification of tumors when requested, but always bearing in mind that the class to which the tumor belongs gives little clue to the prognosis in any particular case.

One objection to the Broders' classification lies in that the grading is solely on the basis of histologic appearance of the cells, and it is a well known fact that no two sections of the same tumor will show exactly the same degree of malignancy. Multiple sections must be taken through various portions of the tumor and the tumor graded according to the average histologic picture. This is a reasonably practical procedure where plenty of time is available, but it is impossible in the case of rapid frozen sections with their limitations as to time and perfection.

Another objection to the classification lies in the fact that the degree of differentiation or of anaplasia does not always correspond to the degree of malignancy, and the pathologist must always bear closely in mind the type of tumor with which he deals, and the location from which it is removed. The cells of a mixed tumor of the parotid gland would certainly show a sufficient degree of anaplasia to rate a grading of 2 or more if found in a tumor of the rectum. We know that an adenoma of the rectum is continually on the verge of malignant change, but histologically the cells appear as benign as the cells of kidney which very rarely become malignant. The cells of a typical squamous cell carcinoma undergo a marked amount of differentiation, whereas the cells of a basal cell carcinoma differentiate very little by comparison, but we are familiar with the fact that the former tumor is more malignant than the latter.

Probably the most serious objection to Broders' classification of tumors lies in the fact that there is little relationship between the grading of the tumor and the prognosis so far as the patient is concerned. The combination of Broders' classification with that of Duke as advocated by Dr. Smith will remedy that defect in the case of grading of carcinomata of the rectum, and a similar classification should be advocated for the grading of all tumors. It is much more important so far as the patient is concerned to know whether the tumor of the rectum has penetrated the rectal wall (Group A, Duke) or has penetrated the rectal wall and has not spread through lymphatics (Group B), or has metastasized to the neighboring lymphatics (Group C), than it is to know whether his tumor belongs to Group 1 or Group 4. Even here we must bear in mind that neither the surgeon nor the pathologist can always tell whether or not a tumor has metastasized. It is my opinion that a combination of the classification of Broders and Duke is an excellent procedure. Broders' classification should give aid in determination of the radiosensitivity of the tumor, and Duke's classification should aid in the determination of the prognosis.

Dr. Curtice Rosser, Dallas, Tex.—I thoroughly agree with Dr. Duke's statement that a superficial biopsy is often deceptive in regard to the actual grade of the tumor, but the use of the electrosurgical unit does make it possible to remove a sufficiently large fragment of the lesion for accurate grading by a competent pathologist in advance of an operative procedure.

Unquestionably there are variations between Broders' grading and Duke's grouping caused by differences between the degree of malignancy present and the amount of resistance to its spread on the part of surrounding tissues. Kerr and I have recently reported a series of young patients with cancer of the rectum in whom we found this variance. Seven of our patients were under 30 years of age. In two, the Broders' grading and the Duke's grouping corresponded. One of these was a Grade 1 adenocarcinoma and fell into Duke's Group A; another, whose tissue was Grade 2, was in the B classification. The remaining five patients were in Group C, that is, the lymphatics were involved. Three of the five showed a low degree of intrinsic activity (Grade 2); one a very low grade of activity (Grade 1); and only one belonged to the Broders' Grade 4 class.

We felt that since this younger group did not show a greater percentage of the higher grades of cancer, we could assume that the earlier spread of the lesion was due to the partial absence of defensive barriers to early spread of intestinal cancer in the young.

Dr. Marion C. Pruitt, Atlanta, Ga.—The chief value of Broders' histologic grading of rectal cancer is its

basis for prognosis of the disease. When a histologic examination is made before operation it may aid in determining the extent and method of surgical procedure. Histologic examination after operation is only of prognostic value.

The findings in the examination of the gross specimen are also only of prognostic value. The clinical findings as determined before and during operation indicate the extent of operative procedure necessary to cure the patient. Therefore I do not consider Duke's classification of sufficient value to justify the effort.

The progress in the cure of cancer of the rectum has been limited almost entirely to surgery. Radiation thus far has been less effective in the cure of rectal cancer than in other parts of the body. In fact, its results are very disappointing and of doubtful value. Electrodesiccation is definitely limited in its scope.

Extirpation of the bowel containing the growth, except in the earliest cases, is not sufficient for a cure, but who is wise enough to trust his judgment in determining the duration or extent of an early cancer? For this reason the lymphatics draining this field must be included in the section.

The earlier the removal of the growth, the better the prognosis. The younger the patient, the graver the prognosis. Few patients under 30 years of age are cured of cancer of the rectum.

Clinically, cancer of the rectum originates in the mucous membrane as a nodular swelling. As it continues to grow, the extent of the local spread of the growth longitudinally and laterally is visible on the surface. The depth of the invasion is indicated by the depth of the ulceration. Thus, a flat projecting tumor as a rule has not spread far beneath the surface, but a deep crater ulcer indicates deep extension in the tissues.

None of the above factors are much, if at all, changed by the histologic grade of the tumor. Also it has been proven that a growth may be histologically classified as Grade 1 now and later change to Grade 2, 3, or 4. In fact, sections from different parts of the tumor taken at the same time may be graded differently. Furthermore, the opinion of pathologists may vary on the same microscopic picture.

Even in the face of the above facts, Broders' histologic grading of tumors is a step of advance in the treatment of cancer. It tends towards unification and classification of our knowledge in the study of cancer and is of sufficiently definite value to be used routinely.

Dr. Smith (*closing*).—I feel that we have a right to ask our pathologist friends to go to a little extra trouble in helping us to determine exactly the extent of spread. I do not feel that we know that unless the lymphatics of a resected specimen are studied up to the inferior mesenteric pedicle. I feel sure that the pathologists are not going to be the first to attack this problem, because, primarily, it is a problem that concerns us and we should ask them to aid us.

This requires extra work, to be sure, but the extra work has its compensatory side in that we actually find out whether or not the lymphatics up as far as we have resected have been invaded by the metastatic process.

AN ELECTRICALLY LIGHTED ANOSCOPE WITH DETACHABLE HANDLE*

By J. H. Dodson, M.D., F.A.C.S.
Mobile, Alabama

This instrument consists of a scope with a detachable handle which contains a battery. It is constructed of brass and chromium plated. The handle is connected at such an angle that the scope can be easily rotated throughout the entire anal circumference regardless of the size of the patient. The light can be switched to either side so as not to obstruct passage of obturator. The thumb of the hand which grasps the handle rests upon the outer end of the obturator, thus facilitating insertion. After withdrawal of the obturator, the same thumb conveniently rests upon the knurled portion which operates light. Contact is made as the lamp is swung into operative position.

*Demonstrated to the Section on Proctology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

MEASLES COMPLICATING PREGNANCY*

REPORT OF TWENTY-FOUR CASES WITH THREE INSTANCES OF CONGENITAL MEASLES

By ISADORE DYER, B.S., M.D.†
Tahlequah, Oklahoma

Measles has long been considered a grave complication if it occurs during pregnancy and there is little doubt that its incidence during pregnancy is even greater than the literature has shown during the past twenty years. During the winter of 1938-39, in the short interval of three months, twenty-four cases were discovered in the rural district included in the five-county demonstration area in northeastern Oklahoma. It is also true that, although in this area there exists an active maternity care program, it would be within reason to suppose that even more instances of the infection escaped our supervision. The occurrence of a rather widespread epidemic over a five-county area provided data which offer a unique opportunity to present comparative figures, some of which are at variance with the information thus far presented in the literature.[2 3]

Selective immunity of the newborn infant to communicable diseases is accepted.[9 10] This immunity is of the passive type and is presumably derived from the mother by means of the placental or mammary transmission of antibodies. Antibodies have been demonstrated in cord and placental blood, which has led to the use of placental extract either to protect an exposed individual or to attenuate the disease after it has occurred. Hence, measles in the newborn is apt to appear rarely in communities where the disease has occurred as one of childhood and thus has permitted the mother to transmit a passive immunity to her offspring. This immunity is almost absolute for the first five months and relative up to the eighth month, at least.[1]

On the other hand, in rural communities, where homes are more widely separated, the disease is more apt to occur in adults, making its appearance in epidemic form over longer intervals, and thereby affecting women during the child-bearing period.

In the present study, the age of occurrence ranged between 14 and 42, with 37.4 per cent appearing after 25 and 16.7 per cent after the age of 35 (*Chart 1*). In practically every infection, the entire family contracted the disease, husband and wife alike, and the mode of transmission as a rule was through one of the school children.

The effects of the disease on pregnancy varied. Uterine contractions occurred in eleven, or 45.9 per cent, which resulted in the emptying of the uterus in nine cases, or 37.5 per cent. Of these, four were primipara and five multipara. Uterine contractions occurred most frequently during the end of the incubation period and on the first day of the eruption. It was noted that six women (in whom the emptying of the uterus was attributed to the disease) had reached or passed the thirty-eighth week of pregnancy (*Table 1*). Of the remaining three, two delivered premature babies at thirty-three weeks and one aborted at eighteen weeks. In the cases seen, the measles was more prone to terminate pregnancy in the last two weeks; the pregnancy suf-

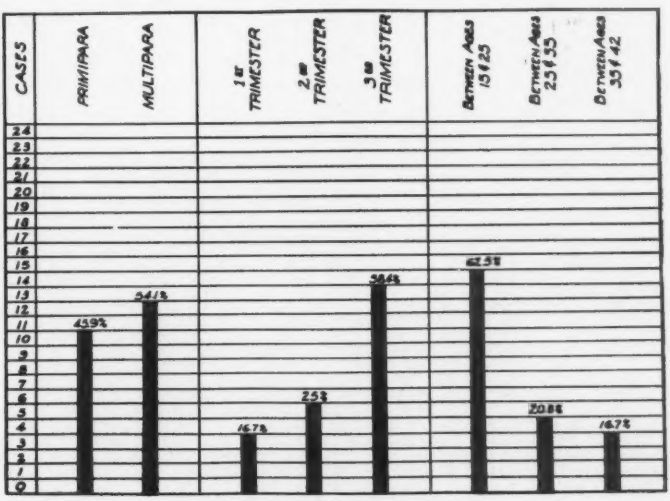


Chart 1
Age incidence of occurrence.

*Read in Section on Public Health, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

†Consultant Obstetrician Cooperative Health District No. 1, Tahlequah, Oklahoma.

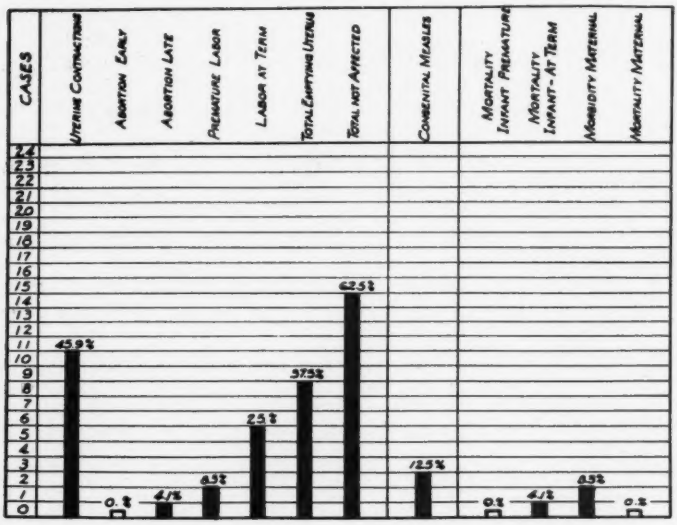


Chart 2
Effect of measles on pregnancy.

fered no ill effects in fifteen, or 62.5 per cent, of the series (*Table 1*).

There were three patients who exhibited sequelae (*Cases 1, 15, 16, Table 1*), namely, residual bronchitis, bilateral otitis media, and a third who developed an anemia, lost weight, and developed fever postpartum. This last was listed as a low grade sepsis, and it was felt that measles occurring at the thirty-fourth week may have enhanced infection by lowering her resistance at the time of delivery at the thirty-seventh week.

There were three instances of congenital measles.

No.	Name	Age	Gravi	Para	Gestation in Weeks	Disease Duration	Effects on Pregnancy	Effects on Mother	Effects on Baby
1	Mrs. C. J.	28	iii	ii	8	10 Days	None	Residual Bronchitis	None
2	Mrs. S. C. E.	39	viii	vi	11	12 Days	None	None	None
3	Mrs. J. H.	38	iv	iii	12	7 Days	Uterine Cramping ~2 to 3 hrs.	None	None
4	Mrs. I. M.	19	i	o	14	8 Days	Uterine Contraction 3 Days	None	None
5	Mrs. R. B.	18	i	o	16	12 Days	None	None	None
6	Mrs. S. P.	39	vi	iii	18	8 Days	Late Abortion 7 Days Following Rash	None	No Rash (Previable)
7	Mrs. H. M.	27	iv	iii	20	8 Days	None	None	None
8	Mrs. E. B.	18	i	o	22	8 Days	None	None	None
9	Mrs. R. E.	35	v	iv	24	12 Days	None	None	None
10	Mrs. R. P.	20	i	o	24	8 Days	None	None	None
11	Mrs. L. S.	25	i	o	27	70 Days	None	Epistaxis	None
12	Mrs. E. H.	23	ii	i	30	8 Days	None (Twin Pregnancy)	None	None (Twins)
13	Mrs. J. H.	22	ii	i	32	14 Days	None	None	None
14	Mrs. M. P.	14	i	o	33	10 Days	Premature Labor 2 weeks after Rash Appeared	None	None — No Rash Premature, 3 Lbs. — Lived
15	Mrs. S. P.	22	i	o	33	7 Days	Premature Delivery 5 Days After Rash	Bilateral Otitis Media	Wt 4 Lbs. — Jaundice No Rash — Lived
16	Mrs. A. B. R.	13	i	o	34	10 Days	None	Postpartum Fever & Sepsis	None
17	Mrs. M. O'N.	21	ii	i	35	14 Days	None	None	None
18	Mrs. S. M.	16	i	o	36	7 Days	None	None	None
19	Mrs. A. W.	33	v	iv	38	10 Days	Labor Began 5th Day of Rash	None	None — No Rash
20	Mrs. N. M.	42	viii	vii	39	10 Days	Labor Began 2nd Day of Rash	None	None — No Rash
21	Mrs. L. C.	19	i	o	39	7 Days	Labor	None	Measles At Birth — Lived
22	Mrs. G. T.	19	i	o	39	6 Days	Labor	None	Measles At Birth — Lived
23	Mrs. E. J.	26	iv	iii	40	10 Days Postpartum	Rash 3rd Day Postpartum	None	None — Rash 2nd Day of Life Died at 1 mo. — Pneumonia
24	Mrs. P. A.	21	v	iv	40	14 Days	Rash 7th Day Postpartum	None	Measles on 14th Day of Life Extraintestinal — Lived

Table 1

The first, Mrs. E. J. (*Case 23, Table 1*), a gravida 4, para 3, was delivered normally at term. A well-defined measles rash appeared in the infant on the second day of life. Twenty-four hours later, the mother developed a measles eruption. The puerperium was normal, except for fever, which subsided in three days after the exanthem reached its height. The progress of this infant was normal. It nursed normally (there appeared no contraindication to nursing the baby), and recovered from the infection. However, at one month of life it expired as a result of pneumonia. There exists a question as to whether or not the pneumonia may have been precipitated by the measles infection.

The second, Mrs. G. T. (*Case 22, Table 1*), a primipara, delivered an infant on the second day after measles had been diagnosed in the mother. The baby exhibited a generalized, coarsely punctate erythema, which covered its chest and abdomen. Koplik spots were present. Its temperature was 102° rectally at birth, but returned to normal (99° rectally) in twenty-four hours and, in forty-eight hours, the exanthem was hardly perceptible. There was an uneventful recovery for both baby and mother.

The third, Mrs. L. C. (*Case 21, Table 1*), presented a difficult problem and is deserving of a case history. She was admitted to service during her seventh month on November 15, 1938; gravida 1, para 0; age 19. On examination she presented normal findings, with the exception of the pelvic measurements. These were: Sp. I 25.5 cms., Cr. I 27 cms., Baud. 17½ cms., Bi-isch 10 cms., Post. Sag. 7 cms, D. C. 9½ cms., and C.V. (estimated) 7½ cms. It was felt that this contraction at the inlet would present dystocia at delivery and plans were made to hospitalize her at the W. W. Hastings Indian Hospital. At the thirty-sixth week the fetal head would not enter the inlet. She was admitted to the hospital on January 23, 1939, in her thirty-seventh week, and x-ray studies revealed a normal baby and confirmed the diagnosis of an antero-posterior contraction at the inlet. An elective cesarean section was planned one week after admittance. Three days later, she informed us that she had slept with a sister who had developed measles, a week prior to her admission. She was isolated and observed: On January 28, 1939, her temperature was 100° and white count 6,200; on January 29, 1939, an exanthematous rash appeared, and her temperature was 101.2°, Koplik spots were present and a diagnosis of measles was made. Labor began with marked intensity and sedation was given at 10:00 p. m. January 30, 1939, at 8:00 a. m., rectal examination revealed three-fourths effacement and dilatation 2 cm., fetal head floating, contractions moderately severe, fetal heart rate 160, membranes intact. At 12:00 noon, her temperature was 103°, she was 3 cms. dilated and effacement was almost complete, pains were severe, sedation of morphine and pentobarbital was given. Fetal heart rate was 140 at 6:00 p. m., the head was still floating and the patient's condition was about the same. Labor pains which had subsided reappeared with intensity. Sedation was repeated; at 12:00 midnight, pains occurred every four to five minutes, there was 4 cm. dilatation, effacement was complete, the fetal head was floating, fetal heart rate 160, and temperature 102°. It appeared then that efforts for 32 hours to stop labor were futile. The outcome, should she continue to dilate and possibly rupture membranes, with the necessity of a craniotomy, was grave. It was felt that laparotrachelotomy under local anesthesia was the procedure of choice. This operation was performed at 2:00 a. m. January 31, 1939, and a 7½-pound infant was delivered. The baby exhibited a marked exanthematous rash, which was most prominent on its chest, abdomen and face, and Koplik spots were present. Its temperature at birth was 101° rectally. Both baby and mother enjoyed an uneventful recovery, the temperature and rash disappearing by February 2, 1939. There was no evidence of sepsis or sequelae in either mother or infant.

Morbidity was observed in only the one patient (*Case 16, Table 1*), who developed a febrile course postpartum. This was three weeks after the measles infection. There was no maternal mortality. The incidence of congenital measles was 12.5 per cent. Infant mortality, if the one infant who developed pneumonia at one month of life is considered, would be 4.1 per cent for the series, and 33.33 per cent for the three instances of congenital measles.

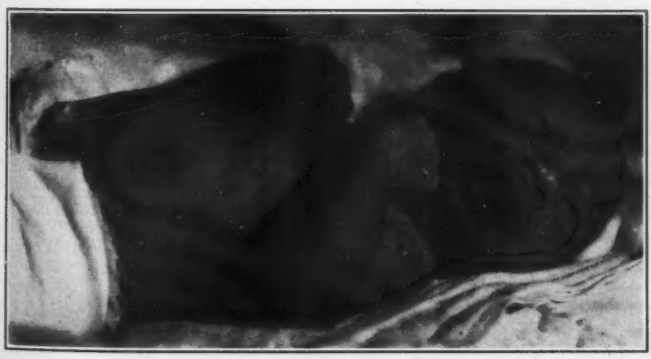


Fig. 1
Baby of Mrs. L. C., four hours after birth.

SUMMARY

(1) Twenty-four cases of measles complicating pregnancy were observed over a period of three months.

(2) Age incidence ranged between 14 and 42 years.

(3) Pregnancy was interrupted in 37.5 per cent, and of these, 25 per cent were at or near term.

(4) Three babies exhibited measles at or two days following birth.

(5) A laparotrachelotomy

was performed on one mother at the height of her exanthem because of a pelvic contraction and persistent labor.

(6) There was no maternal mortality, but one instance of morbidity due to sequela.

(7) Measles during pregnancy probably occurs more commonly than the literature, reviewed for the past twenty years, would show.

(8) The effects on pregnancy were not so serious in this study as is indicated in the literature.

BIBLIOGRAPHY

1. Brennemann, J.: Practice of Pediatrics (Robert A. Strong), 2: Ch. 11, 2. Measles. Hagerstown: W. F. Prior Co., 1938.
2. DeLee, J. B.: Principles and Practice of Obstetrics, 7th Ed., p. 551. Philadelphia: W. B. Saunders Company, 1938.
3. Stander, H. G.: Williams' Obstetrics, 7th Ed., p. 647. New York: D. Appleton-Century Co., 1936.
4. Curtis, A. H.: Obstetrics and Gynecology, **1**:997. Philadelphia: W. B. Saunders Company, 1933.
5. Nouvat, J. R.: Roureole et Grossesse: Th'se de Bordeaux, 1904.
6. Tow, A.: Diseases of Newborn, p. 337. Oxford Med. Pub., 1937.
7. Von Reuss, A. R.: Diseases of Newborn, p. 482. New York: William Wood, 1922.
8. Kohn, J. L.: Measles in Newborn Infants (Maternal Infection). Jour. Pediat., **3**:176-180 (July) 1933.
9. McKhann, C. F.; and Chu, F. T.: Measles: Use of Placental Extract. Amer. Jour. Dis. Child., **45**:475-479 (March) 1933.
10. McKhann, C. F.; and Coady, H.: Measles: Prevention in Infants. Sou. Med. Jour., **27**:20-24 (Jan.) 1934.
11. Richardson, D. L.: Measles Contracted in Utero. Rhode Island Med. Jour., **3**:13 (Jan.) 1920.
12. Ronaldson, G. W.: Measles at Confinement with Subsequent Modified Attack in Child. Brit. Jour. Child. Dis., **23**:192-195 (July, Sept.) 1926.
13. Karelitz, S. S.: Prophylaxis Against Measles. Amer. Jour. Dis. Child., **55**:—, 1938.
14. Phillips, W. R.: Amer. Jour. Dis. Child., **55**:1257, 1938.

DISCUSSION (*Abstract*)

Dr. Robert A. Strong, New Orleans, La.—It is not necessary for me to invite the attention of a group of this type to the fact that of all the communicable diseases with which we have to deal, measles is by far the most widely prevalent, and being more contagious as well, it spreads with great rapidity from the patient to any susceptible contact. In recent years, there has been an approximate annual average of 400,000 cases reported in the Registration Area of the United States, and it is reasonable to assume that about twice that number occur, but are not reported. Consequently, the paper that Dr. Dyer has just presented to us is of particular interest, because not only does it reveal an unusual manifestation of the disease, but it corroborates well defined impressions on immunity and susceptibility.

The contagiousness of measles and the individual susceptibility to it make its control one of the most perplexing problems in preventive medicine. Few persons escape acquiring it in childhood or before reaching adult life, and those who do not have the disease in early life may become victims of it during any epidemic if they are exposed to infection. In exemplification of this fact, an epidemic of measles among boys from rural areas occurred in almost every cantonment during the World War. However, since the widespread use of the automobile and intercommunication between rural and urban areas, and the establishment of the consolidated school system, the opportunity for young children to acquire the disease is greater than formerly.

One of the most interesting phases in the incidence of measles is brought out in Dr. Dyer's report, and that is its occurrence in the offspring of mothers who developed measles either shortly before or at delivery. It is known that babies under six months of age invariably possess an immunity to measles, provided their mothers have acquired one by an attack of the disease previous to pregnancy or several months before delivery. Theoretically, this immunity may be acquired by the newborn either through the placental transmission of an antigen sufficiently potent to stimulate a limited active immunity, which lasts for at least five months and maybe as long as eight months, or through placental antibodies capable of producing a passive immunity for the same length of time. The continuation of this passive immunity, which ordinarily is of short duration, may be extended by some unknown factor, which may be the specific resistance, said to be possessed by rapidly growing tissues, called "tissue immunity." While Dr. Dyer's report does not disprove these facts or theories, it definitely proves the possibility that an offspring of a mother with measles may develop the disease. Working on the basis of a placental transmitted immunity possessed by newborn babies to communicable diseases in general and measles in particular, McKhann and his associates, in Boston, prepared a saline extract from ground-up, pooled placentas of Wassermann-negative and Kahn negative mothers who had previously had measles. After freeing this extract of gross tissue and blood cells, they precipitated it with ammonium sulphate, dialyzed it to remove salts, adjusted it for protein-hydrogen content, and preserved it with phenol. In a later study, they refined and concentrated it, and although some of its potency was lost, it was rendered safer by freeing it from some of the elements responsible for reactions which were sometimes severe. This preparation was first announced in 1933 and sufficient time has elapsed for its clinical trial for the purpose of preventing or modifying measles. It may be said to compare favorably in effectiveness to convalescent serum and because it contains nothing other than what is found in convalescent serum, the immunity conveyed is passive in type and consequently of short duration. It appears to be as useful as convalescent serum, with the additional advantage of being conveniently available when needed, and whereas its use can seldom prevent the disease, the attack may be modified. Immune globulin (human) has fulfilled the requirements of and has been accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

Dr. Dyer (*closing*).—I am glad to hear Dr. Strong emphasize the existence of this condition in a rural community.

CEREBELLAR ABSCESS*

REVIEW OF CASES

By HARRY WILKINS, M.D.
Oklahoma City, Oklahoma

Within recent years many new facts relative to the problem of brain abscess have been clarified. These inflammatory processes were recognized more than a century ago and accurate data were recorded even pertaining to localization within specified areas such as the cerebellum. An excellent description of the clinical symptoms of a cerebellar abscess occurring in a girl of 9 years, observed by Abercrombie[1] as early as 1810, is recorded in his "Diseases of the Brain," printed in 1828. The postmortem findings in this and another case observed by him in 1813 are characteristic of present day reports of abscess in this region. Describing the gross pathology in a case, he says:

"A considerable quantity of colorless fluid was found in the ventricles of the brain. In the left lobe of the cerebellum there was an abscess of considerable extent, containing purulent matter of intolerable foetor. The dura mater, where it covered this part of the cerebellum, was thickened and spongy, and the bone corresponding to this portion was soft and slightly carious on its inner surface; but there was no communication with the cavity of the ear."

In each of his cases the origin of infection was a chronic otitis. Naturally at that time, surgical intervention had not been resorted to in the management of these cases. It was not until 1886 that an accurate diagnosis with a well planned and well executed operation was employed with success in the treatment of a cerebral abscess. The credit for this belongs to Barker and Bowers, as mentioned by Davidoff.[2] The problem of management of local purulent encephalitis of the cerebellum remained highly distressing due to the high mortality rate in such conditions as indicated by the St. Thomas Hospital report covering a period of five years from 1899 to 1904 (reported in an article by Davidoff[2]). Among 19 cases of brain abscess with seventeen deaths, there were seven cases of cerebellar abscess with six deaths. This impression of the mortality rate with abscess in this region persists in the textbooks of recent date (Wechsler[3]).

Within the past few years detailed reports from the study of this problem cast a ray of hope heretofore lacking. Adelstein,[4] in an instructive review of the problem, points out the fact that in their series of abscesses of the brain of otitic origin, the abscess was found in the cerebellum in the ratio of one to two in the temporal lobe. Furthermore, Courville and Nielsen[5] in 10,000 necropsies found that 46 per cent of all brain abscesses were of otitic origin. The long-standing impression that the mortality rate is extremely high is refuted by the experience of Atkinson,[6] Adelstein[4] and others. Bucy[7] has the enviable record of five cases surgically treated without a death.

The first case of abscess within the cerebellum encountered by my associate and me was in our clinic in 1933. Lacking the assurance offered by the reports of subsequent date, we naturally maintained a pessimistic attitude. We believe that this attitude was engendered by fear of the danger of meningitis. This fear was thought to be justified by anatomical factors encountered. With additional experience we have had rather encouraging results in the surgical management of these cases, and in reviewing our series and in comparing the methods employed with those used in handling cerebral abscesses, we believe that the anatomical factors probably work in our favor and contribute to results permitting a more optimistic attitude when one encounters a lesion of this character.

The mechanical factors incident to expansion of a lesion confined within the relatively small posterior compartment of the cranial cavity tend to facilitate evacuation of the abscess and obliteration of the cavity rather promptly when drainage is established. Likewise, the relative size of the abscess and that of the posterior fossa favor a positive pressure which aids in sealing off the subarachnoid spaces, thus tending to prevent a spread of infection within the meninges.

The structure of the cerebellar cortex would seem to favor formation of an adequate capsule. As pointed out by Penfield,[8] the presence of vascular structures and pia favors fibroblastic proliferation. Why, then, should we not expect favorable conditions for capsule formation, since with the large number of folia there is an abundance of mesodermal tissue present? Furthermore, the tendency for the abscess to form within a single folium and remain confined to that structure, as described by Atkinson,[6] would tend to favor early limitation of the purulent

*Read in Section on Neurology and Psychiatry, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

process. When the abscess occurs within the central white matter, certainly the conditions are less favorable, as will readily be recognized in one of our fatal cases (*Fig. 1, Case 14*).

In this series of cases we share the experience of others that the sources of infection are predominantly the middle ear, mastoid, and petrous cells. We have encountered four cases of non-otogenous origin and the results in treatment of these have been far less satisfactory on the whole than in the laterally placed abscesses.

In searching for the cause of failure in treatment, we find that these lesions were situated deep within the white matter of the hemisphere or within the ventricle. We believe that the lack of tissue response to the infection accounts for inadequate encapsulation, and the tissue failure is dependent on the absence of vascular and mesodermal tissues that contribute to formation of the abscess wall. It has been the consensus of opinion of neurosurgeons that the success with drainage of abscess of the brain is dependent to a great degree upon the ability of the tissue to produce a capsule and the passage of sufficient time for the process to reach completion (Adson and Craig,[9] Grant[10]).

The routes of infection from the middle ear and mastoid favor the formation of the abscess in the more favorable cortical tissue. As pointed out by Atkinson[6] and others, four pathways must be taken into account. The lateral sinus may become thrombosed by direct contact with the infected mastoid. From this source the perisinus abscess, or localized meningitis, may be followed by extension to the brain along a thrombosed vein or by way of a perivascular space. Numerous venous connections laterally placed in the posterior fossa, favor the extension of infection to the adjacent cortical structures both from the sinus or directly from the mastoid or petrous cells without involving the transverse or sigmoid sinus. Direct extension through Troutman's triangle is not uncommon. Infection has been seen to follow along the fallopian canal, but this is unusual and is almost invariably associated with an infranuclear type of homolateral facial paralysis. From the labyrinth the infection may reach the cerebellum by local destruction of bone or by passage along the aqueduct of the cochlea or the ductus endolymphaticus.

Fig. 1
Multilocular abscess deep within cerebellar hemisphere (Case 14).

SYMPTOMATOLOGY

The symptoms during the stage of invasion are not unlike those of abscess formation elsewhere in the brain. Headache is an outstanding symptom, and tends to occur both in the suboccipital and frontal areas. A septic temperature, leukocytosis with a relative polymorphonuclear cell increase, meningeal signs, rapid pulse, and associated systemic manifestations are present. As the process of encapsulation occurs these systemic manifestations recede, but the headache tends to persist. Because of the interference with cerebrospinal circulation, general pressure signs develop rather early and choked disc is much more frequent than in cases of cerebral abscess. With encapsulation and enlargement of the abscess, characteristic unilateral cerebellar signs develop. Nystagmus predominantly to the homolateral side with ataxia and dysdiadokokinesia, on the same side may be associated with muscular hypotonia. Loss of muscle check and staggering gait with tendency to deviate to the side of the lesion occur with regularity. In those abscesses situated deep within the white matter, localizing signs have, in our cases, been less frequent, although the contrary would seem the rule from the fact that nystagmus and other cerebellar signs arise as a result of nuclear involvement. When the lesion is well forward, signs rather typical of the cerebellopontine angle tumor may be noted (*Case 2*).

As mentioned by Atkinson,[6] one must consider the following conditions in differential diagnosis:

(1) Acute suppurative labyrinthitis.

(2) Frontal lobe abscess.

(3) Cystic serous meningitis.
(4) Tuberculous menigitis.
(5) Tumor.

In addition, we feel that pseudo-abscess or otitic hydrocephalus should be considered. In the majority of cases, careful analysis of the history and neurologic findings will suffice in differentiating the abscess from these conditions. Examination of the spinal fluid lends additional worth-while information in the ill defined cases. A word of warning might be given here that spinal puncture is particularly dangerous in abscess of the cerebellum, as it is in cases of tumor within the posterior fossa. In our clinic, spinal punctures are rarely done unless pressure signs are absent and even then we recognize that the procedure is not without hazard, as evidenced by one of our cases (*Case 14*). Surgical exploration for the abscess or ventriculography may, at times, be found necessary before a final diagnosis can be reached. It is our belief that exploration is less dangerous than ventriculography when the exploration is carried out by an approach through a clean field.

TREATMENT

Numerous questions confront one in the management of cerebellar abscesses as in brain abscesses situated elsewhere. These have been outlined by Davidoff.[2] Certain questions have been definitely settled, namely, when to operate and whether to approach the lesion through a clean field or follow the pathway of infection. Certainly everyone agrees that the optimum time for operation is when encapsulation has occurred. The dispute as to the route of approach was settled as early as 1912, when Sir Victor Horsley declared that it should be through the mastoid when the adjacent dura was eroded and through a clean field if a definite preformed pathway was not encountered. Other questions remain unanswered and rather than enter into a controversy as to the method of drainage, the nature of the drain, the postoperative management and other details, I shall give the method resorted to in our clinic and let the results speak for themselves. We do not claim originality in our method of management.

We join with Wails,[11] Mayfield and Spurling[12] in advocating removal of the primary foci of infection. Lund[13] reports that 80 per cent of abscesses of otitic origin develop in cases of chronic infections of the ears, which suggests that the otologist might be mindful of the advantage to be gained by the removal of such foci even as a preventive measure more often than has been done in the past. In our work we have had excellent cooperation from our otologists. In some instances the mastoid operation has been carried out before, in others at the time of, and in still others following the drainage of brain abscess. Factors in the given case must guide one in this matter.

It has been our custom to perform the operation in the reclining cerebellar position. A vertical incision, approximately three centimeters in length, is made in that area just below the transverse sinus and medial to the vertical portion of the sigmoid sinus after having isolated the mastoid wound, if one exists, from our clean field (*Fig. 2*). This incision may be modified to gain room by a mesial extension at the superior end of the incision. The bone is exposed by incision of the fascia and muscle. A perforator and burr opening is adequate for exploration with a ventricle cannula. Thorough exploration is necessary, lest one miss the abscess as we did in *Case 4*, in which instance the result was a fatality. Specimens of pus are taken for direct smear and culture when pus is encountered. When the pressure is lowered by the escape of pus, so that it does not force its way out through the needle tract, the cannula is removed and the opening sealed with a small plaque of cottonoid. The bone defect is then enlarged to approximately 2.5 centimeters in

Fig. 2
Site of skin incision. Transverse sinus indicated by dotted lines.

diameter, which suffices for our particular method and type of instruments.

The dura is incised to the limits of the bone defect and the subarachnoid space sealed off by a single circular strip of ½-inch iodoform gauze. A channel approximately one centimeter in diameter is made through the overlying cortex with the rigid suction tip and a longitudinal slit is made in the exposed abscess wall (*Fig. 3*). The excess of pus is controlled by its removal with suction, allowing the tip of a narrow retractor to be inserted into the cavity, giving adequate exposure and preventing collapse of the cortex and subarachnoid contamination. As a rule, the pus is completely evacuated and a section of firm rubber tubing one centimeter in diameter and fenestrated at its lower end is inserted to the bottom of the cavity.

Four strips of ½-inch iodoform gauze are inserted alongside the tube, one in each quadrant and sufficient gauze is used to keep the cavity from collapsing (*Fig. 4*). These strips of gauze are gradually withdrawn at the time of subsequent dressings, a process requiring as a rule ten days to two weeks. The circular strips of iodoform gauze used to seal the subarachnoid space and additional circular packing used to hold the muscle and skin wound open, can be removed within a week. With each dressing, the tube is rotated and its lumen cleared by using an applicator wrapped with cotton to the diameter of the lumen of the tube. Gradually, as the tube is extruded, the protruding portion is removed with scissors and within two to three weeks the tube can be removed, cleansed and replaced without danger of producing a false passage. The complete extrusion of the tube usually occurs within from three to six weeks (*Fig. 5*). In only one instance was it found necessary to redrain the area (*Case 10*).

In addition to the surgical removal of the original focus and drainage of the abscess, general suppurative measures are necessary, and with the advent of chemotherapy we have found administration of sulfanilamide and sulfapyridine worthy of use as prophylaxis for meningitis, the chief pitfall in surgical treatment of brain abscess.

In four of our cases of otitic cerebellar abscess, either at the time of operation or within a few days thereafter, cerebrospinal fluid has escaped from the tube. One must guard against dehydration in such an event as the fluid loss is excessive, but no untoward effects have occurred and we share Bailey's[14] belief that this, after all, is not a catastrophe as was formerly thought to be the case.

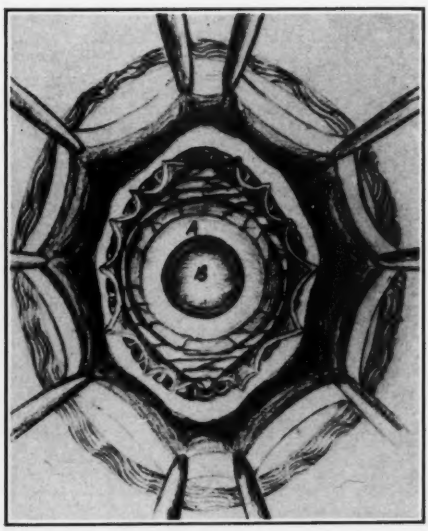


Fig. 3
Abscess wall exposed and incised. (A) Abscess wall. (B) Abscess cavity.

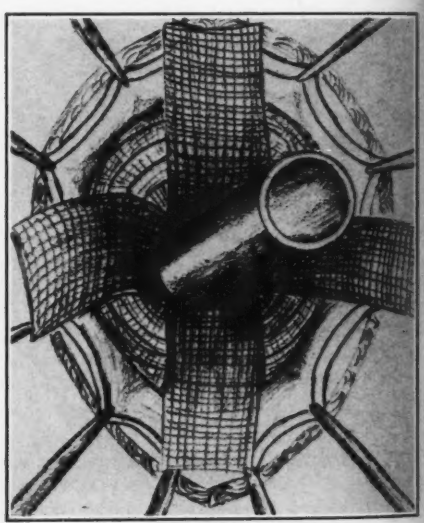


Fig. 4
Tube in place. Note circular gauze and iodoform wicks.

SUMMARY OF CASES

This series of cases represents all of the cerebellar abscesses encountered in our clinic from 1933 to the present. My associate, Dr. J. D. Herrmann, and I have each observed them and we have shared in the responsibility of surgical treatment.

A detailed report of *Case 1* will serve as a fairly typical example of the symptomatology, progress, and surgical procedures resorted to in these cases. The accompanying *Table 1* summarizes the entire series. *Table 2* gives a summary of statistical data. (*Tables 1* and *2* on next page.)

Case 1.—J. H., a white boy, aged 10 (St. Anthony's No. 80215), on April 18, 1933, was referred by Dr. Roy Emanuel, of Chickasha, Oklahoma.

He had acute otitis of ten days' duration, mastoiditis, intracranial pressure and left cerebellar signs. Mastoidectomy was done, and three days later drainage of a cerebellar abscess, with complete recovery.

His illness had begun March 20, 1933, with high fever and systemic distress thought to be influenza. He developed left otitis media and the drum ruptured spontaneously. On the tenth day after onset, that is, April 1, he vomited, complained of constant headache and then became stuporous. His symptoms were persistent and increasing until admission, 18 days from the onset of symptoms of intracranial complication.

Fig. 5

Case No. 12. Thirty days postoperative. Tube extruded.

On examination the boy was stuporous, but could be aroused. His temperature was 99°, pulse 62, and low grade papilledema was present bilaterally. There was nystagmus to the left; the pupils were equal; there was no strabismus. Ataxia of the left arm and leg were present. There were no pyramidal pathway signs. The white blood count was 23,500, with neutrophils 78 per cent.

For three days repeated respiratory episodes occurred, associated with tonic convulsions characteristic of decerebrate rigidity. Spinal puncture just preceding operation revealed a cell count of 18 leukocytes, 90 per cent neutrophils, and 10 per cent lymphocytes. Culture was negative.

On April 21, 1933, a mastoidectomy was done by Dr. L. C. McHenry. A small extradural abscess was encountered and a direct smear was reported as showing many streptococci. His general condition improved, but left lateral cerebellar signs persisted and the papilledema advanced. April 24, 1933, the twenty-fourth day from the onset of intracranial signs, a left cerebellar abscess, well encapsulated, was exposed and drained. He was up in a wheel chair May 12, 1933, and discharged May 18 with tube removed. Persistent drainage from the left ear necessitated tonsillectomy and adenoidectomy and curettement of the mastoid wound. Rapid improvement and recovery occurred without residual signs of intracranial pressure or localized cerebellar phenomena.

This is a rather typical experience of the acute otitic infections complicated by abscess within the cerebellum. Drainage of the abscess was postponed until encapsulation had taken place.

CONCLUSIONS

(1) A large percentage of cerebellar abscesses are of otitic origin; 64 per cent in this series.

(2) The physical principles encountered and the presence of an abundance of tissue of mesodermal origin probably account for the tendency of these infections to become localized and encapsulated.

(3) Removal of the primary focus is of paramount importance in the management of these cases.

(4) The morbidity in the cases recovering is much less than in supratentorial abscesses.

BIBLIOGRAPHY

1. Abercrombie, John: Pathological and Practical Researches on Diseases of the Brain and the Spinal Cord. Edinburgh: A. Balfour & Co., 1828.
2. Davidoff, Leo M.: The History of the Surgical Treatment of Otogenic Abscess of the Brain. **45**:295 (April) 1935.
3. Wechsler, I. S.: A Textbook of Clinical Neurology. Philadelphia: W. B. Saunders Co., 1930.
4. Adelstein, L. J.: Surgical Management of Otogenous Abscess of the Brain. Arch. Otolaryng., **29**:624 (April) 1939.
5. Courville, C. B.; and Nielsen, J. M.: Intracranial Complications of Otitis Media and Mastoiditis. Acta Oto-Laryng., **21**:19, 1934.
6. Atkinson, Miles: Otogenous Cerebellar Abscess. Ann. Otol., Rhinol. & Laryng., **47**:1020 (Dec.) 1938.

TABLE 1—CEREBELLAR ABSCESS: FOURTEEN CASES

Case No.	Date	Name	Hospital and Number	Age	Location	Organism
1	4/24/33	J.H.	St. Anthony 80215	10 yrs.	Left hemisphere	Streptococcus
2	4/19/33	A.J.	St. Anthony 79874	49 yrs.	Rt. cerebellopontine angle	No growth on culture
3	2/17/34	O.F.	St. Anthony 84114	33 yrs.	Right hemisphere	Undetermined
4	5/26/34	D.P.	Univ. Hospital 74425	8 yrs.	Left hemisphere	No growth on culture
5	3/ 3/35	E.C.	Univ. Hospital 79345	20 yrs.	Left hemisphere	Staphylococcus
6	5/ 3/35	W.M.	St. Anthony 92065	12 yrs.	Left hemisphere	Staphylococcus
7	9/26/35	L.C.	St. Anthony 94237	18 da.	Fourth ventricle	Staphylococcus
8	11/27/35	E.J.	Border Hospital Mangum, Okla.	10 yrs.	Left hemisphere	Streptococcus
9	12/28/36	J.McT.	Wesley Hospital N8361	13 yrs.	Right hemisphere	Streptococcus
10	5/ 9/37	B.M.	St. Anthony 99623	10 yrs.	Left hemisphere	Streptococcus
11	5/11/38	F.McC.	St. Anthony 115541	33 yrs.	Deep within left hemisphere	Staphylococcus
12	5/22/39	M.S.	Univ. Hospital	9 yrs.	Right hemisphere	Staphylococcus
13	7/27/39	T.G.	St. Anthony 126744	8 yrs.	Right hemisphere	Streptococcus
14	9/17/39	R.L.H.	Univ. Hospital	13 yrs.	Right hemisphere	Undetermined

Table 2

(A) CEREBELLAR ABSCESS: ETIOLOGY

Otitic		9, 64 per cent
Acute	4, 44 per cent	
Chronic	5, 56 per cent	
Non-otitic		5, 36 per cent
Generalized osteomyelitis	1	
Peritonsillar abscess	1	
Furunculosis, cervical	1	
Staphylococcus meningitis, unknown origin	1	
Origin undetermined	1	
Total		14, 100 per cent

(B) CEREBELLAR ABSCESS: MORTALITY

Otitic		9
Surgically treated	8	
Verified and drained	7, no deaths	
Unverified	1, 1 death	
Non-surgical	1, 1 death	
Non-otitic		5
Surgically treated	3, 1 death	
Non-surgical	2, 2 deaths	
Total deaths	5, 36 per cent	
Total recoveries	9, 64 per cent	
Total cases		14

7. Bucy, P.: The Treatment of Brain Abscess. Ann. Surg., **108**:961, 1938.
8. Penfield, W.: Principles of the Pathology of Neurosurgery. Nelson's Loose-leaf Living Surgery. New York: Thomas Nelson & Sons, 1927.
9. Adson, A. W.; and Craig, W. McK.: The Surgical Management of Brain Abscesses. Ann. Surg., **101**:— (Jan.) 1935.
10. Grant, F. C.: The Mortality from Abscess of the Brain. J.A.M.A., **99**:550 (Aug. 13) 1932.
11. Wails, T. G.: A Rational Method of Treatment of Cerebellar Abscess. Unpublished paper presented before the Oklahoma City Academy of Medicine, November 6, 1939.
12. Mayfield, F. H.; and Spurling, R. G.: Brain Abscess. Stan. Med. Jour., **30**:191 (Feb.) 1937.
13. Lund, R.: Diagnosis and Differential Diagnosis of Otogenous Brain Abscess. Acta Oto-Laryngology, **11**:479, 1927.
14. Bailey, P.: Personal communication.

DISCUSSION (*Abstract*)

Dr. Joseph E. J. King, New York, N. Y.—Until about two decades ago the term "cerebellar abscess" was almost synonymous with death. Up to that time no one had reported a real series of recoveries. There was an occasional report of a recovery, but it was considered accidental and merely good fortune. Anyone who can report a series of nine cerebellar abscesses with almost 100 per cent recoveries, eight out of nine, deserves a great deal of commendation.

We may differ a little in the details of our operative procedures, but on the whole they are very similar.

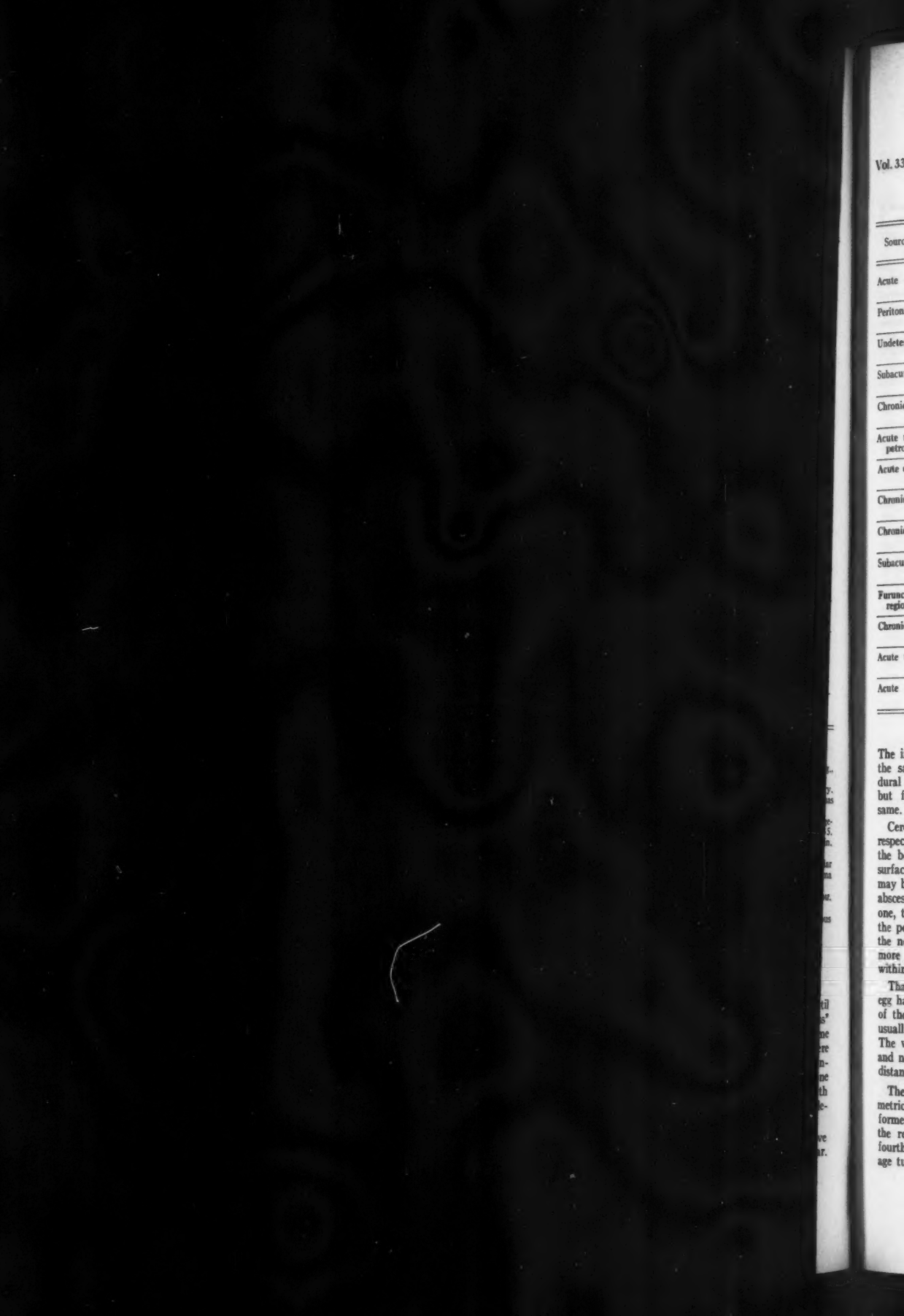


Table 1 (Continued)

Source of Infection	Operation	Tube in Place	Results	Postmortem Findings
Acute mastoid	Mastoidectomy and Dr. Br. abscess	24 days	Complete recovery	
Peritonsillar abscess	Drainage of brain abscess	.....	Death eighth p. o. day	Autopsy denied
Undetermined	No operation	.....	Death third day from onset of symptoms	Acute purulent encephalitis localized to right hemisphere
Subacute mastoid	Cerebellar and temporal lobe neg. exp.	.....	Death tenth p. o. day	Mastoiditis and localized left hemisphere abscess
Chronic mastoid	Mastoidectomy and Dr. Br. abscess	38 days	Complete recovery	
Acute mastoid and petrositis	Mastoidectomy 5/4 Dr. Br. abscess 5/18	15 days	Complete recovery	
Acute cold; age 4 da.	Ventricle puncture and spinal puncture	.....	Death twenty-ninth day of hospitalization	Empyema fourth ventricle and basilar meningitis
Chronic mastoid	Mastoidectomy 11/10 Dr. Br. abscess 11/27	23 days	Complete recovery	
Chronic mastoid	Mastoidectomy 12/31 Dr. Br. abscess 1/18	24 days	Complete recovery	
Subacute mastoid	Exp. Rt. cereb. neg. and Dr. Lt. Abc. 5/9	17 days	Complete recovery	Mastoidectomy left and redrainage of abscess 5/27
Furunculosis cervical region	Craniotomy Abs. unver. 5/16 Dr. Br. Abc. 7/2	37 days	Recovery and out of hospital	Death 8 mos. later. Autopsy revealed refilling of abscess
Chronic osteomyelitis	Drainage of rt. cerebellar abscess	29 days	Complete recovery	
Acute mastoid	Mastoidectomy 7/23 Dr. Br. abscess 7/27	34 days	Complete recovery	
Acute mastoid	Mastoidectomy 5/15 Sec. same 7/10 No Br. Op.	———	Death 13 hrs. following spinal puncture	Deep-seated abscess with multiple cavities, nonencapsulated

The incisions are placed at the same positions and for the same reasons. It is probable that the bony and dural openings which I make may be somewhat smaller, but fundamentally the principles are practically the same.

Cerebellar abscesses are like cerebral abscesses in this respect: that there may be two types with re'ation to the bone. One may approach very near to the brain surface, or even be attached to the bone, while the other may be some little distance from the surface. Cerebellar abscesses are usually, but not always, one of two types: one, the shape of a robin's egg, is securely attached to the posterior surface of the petrous pyramid, usually in the neighborhood of the semicircular canal; the other, more circular in shape, is located in a central position within the cerebellar lobe.

That abscess which is usually the shape of a bird's egg has its smaller pole attached to the posterior surface of the petrous pyramid, while its larger posterior pole usually approaches the dura to within 1 or 1.5 cm. The wall of the abscess which is more centrally placed and not attached to the petrous pyramid may be more distant from the dura.

The operation for cerebellar abscess, I think, is diametrically opposed to that for cerebral abscess. In the former one does not have to consider the ventricle for the reason that there is no ventricle, other than the fourth, in the posterior fossa. We use two small drainage tubes, the size of a Dakin tube, and place them at the bottom of the cavity. In the cerebellar abscess, one does not desire herniation for fear of torsion of the brain stem. Elevation of the floor of the cerebellar abscess, likewise, is not desired as it is in cerebral abscess, for the reason that its attachment to the petrous pyramid probably would be torn away, followed by development of meningitis and death. It is due, not so much to the mere presence of the localized abscess cavity in the cerebellar lobe itself, but to the fact that the lobe is enlarged by the presence of both the abscess and the surrounding edema, both of which compress the aqueduct and produce internal hydrocephalus. The presence of the hydrocephalus is what causes the headache, vomiting, and is what makes the patient sick. By the time the neurosurgeon sees a case of cerebellar abscess, the patient is usually quite ill and has considerable dilatation of the ventricles. Some are in coma or deep stupor. Most of my cases have been in younger people.

Preliminary to any operative procedure, we always puncture the anterior horn of the same side through a burr hole and a nick in the dura in order to decompress the ventricles by removal of intraventricular fluid. Following ventricular puncture the patient is not very ill, and in fact frequently becomes wide awake. Rather than operate immediately, we usually tap the ventricles once or twice in order to allow readjustment of intracranial pressure and the pressure on the brain stem.

In a case of cerebellar abscess all the external work

associated with mastoid disease should have been properly performed, with drill and curette and without hammer and chisel. Sir William Macewen warned against hammering in 1893. A lumbar puncture should not be done for fear of herniation of the conus through the foramen magnum. Once this herniation or jamming of the conus occurs, death is almost sure to follow, and one must always warn against therapeutic lumbar puncture in this condition.

At the time of doing the ventricular puncture a small amount of air is usually substituted for the fluid, and on the anterior-posterior view one will observe symmetrical dilatation of the ventricles, that is, both lateral and third, without displacement. In the posterior-anterior view, the posterior horn on the homolateral side will usually be observed to be smaller than that of the opposite side. This is due to the pressure transmitted through the tentorium by the enlarged cerebellar lobe.

Dr. Moses Keschner reported a series of 24 cases of posterior fossa lesions. Twenty-one showed homolateral signs, two were contralateral, and one gave bilateral signs. Although we usually feel fairly sure of the lobe involved, it is well to corroborate this opinion by ventriculograms.

The incision made by us is probably a bit shorter than that of Dr. Wilkins. It is placed vertically, over the outer portion of the cerebellar lobe, and is through a clean area. It is not believed that an abscess is properly drained through the anterior approach, but in the instance of a direct tract leading into a cerebellar abscess anteriorly, one might be justified in draining, at least temporarily, through this site. It is most important that exploration with a needle should not be made through an infected dura. In the first place, the abscess can be more adequately drained posteriorly, and in the second place, if no abscess already exists, it is almost sure to follow.

Dr. Nicholas Gotten, Memphis, Tenn.—Few neurologic surgeons have had such good results as Dr. Wilkins, and it can be accounted for by his understanding of the principles involved in brain abscess formation.

Every infection about the ear and mastoid bone should be considered a potential source for abscess formation, and that point should be kept in mind. Secondly, once there is evidence of abscess formation, operation should be postponed as long as possible in order to insure encapsulation. Dr. Wilkins has stressed the readiness with which the cerebellum responds to infections in producing a capsule around the abscess.

The symptoms of cerebellar abscess are familiar to all neurologists and need not be reviewed, but the signs for operation do require emphasis. A gradual slowing of the pulse and a marked rise in pressure of the cerebrospinal fluid, or drowsiness, are indications that operation cannot long be deferred. Until these signs are present, watchful waiting should be followed. In differential diagnosis, cystic serous meningitis has caused me more trouble than any other condition. I have seen focal symptoms from such lesions, making differential diagnosis very difficult.

No comment is permissible as to the operative methods outlined by Dr. Wilkins, as his record of recovery speaks for itself. Any method that gives such good results is to be commended.

Dr. Dean H. Echols, New Orleans, La.—During the past five years at the University Hospital in Ann Arbor, Michigan, where 500 neurosurgical operations are done a year, there has not been a single cerebellar abscess. I was not there all of that time, but learned that fact from Dr. Braden last week.

During the two years that I have been in New Orleans, I have not seen a single cerebellar abscess either at the Charity Hospital or in private hospitals. A neurosurgical colleague of mine told me last week that in his twelve years of practice in New Orleans he had never seen a cerebellar abscess except at autopsy. I tell you this to emphasize what an amazing experience Dr. Wilkins has had.

Moreover, although his paper has been modestly presented, the fact that nine of his eleven brain abscesses are living and well is absolutely astounding.

Dr. Hermon S. Major, Kansas City, Mo.—I wish to bring to your attention a plan that we adopted recently at the Kansas City General Hospital in which a closer correlation has been brought about between the department of neuropsychiatry and the department of neurosurgery, to the end that every neuropsychiatric patient is seen by the neurosurgeon and every neurosurgical case is seen by the neuropsychiatrist. We have a rotating service. The neuropsychiatrist is director every two years, and the neurosurgeon may become a director of the department every two years.

It seems to me that the same plan would be applicable to our department in the Southern Medical Association. I am not being subsidized by the neurosurgeons by any means, but they are given no recognition whatever. This is the Section on Neurology and Psychiatry. Why should it not be the Section on Neurology, Psychiatry and Neurosurgery? One of the discussants was talking about having his pin feathers picked out by one of the neurosurgeons back there. It seems to me they have a complaint coming.

Dr. Wilkins (closing).—It has been our good fortune to have the cooperation of our otolaryngologists, who have worked in conjunction with us in all of the cases of otitic origin. With this arrangement we have been able to observe the patient, have the focus of infection removed, and drainage of the abscess instituted at the proper time to give optimum results.

I appreciate Dr. King's remarks on the location of cerebellar abscesses. There are numerous details which I have not discussed because of lack of time. It will be noted that in this series of cases only one above the age of 14 years was encountered. She was 20 years of age. We, therefore, feel that this disease predominates in young people due to the frequency of occurrence of otitic infections in childhood.

Dr. King's remarks relative to ventricle puncture are timely. I agree with him that this procedure is to be evidenced with benefit during the period in waiting for proper encapsulation, as the relief of intracranial pressure by this method is far safer than by resorting to spinal puncture. Evidenced in conjunction with more conservative methods of relieving the intracranial pressure, it seems a definite adjunct to safety in treatment. In our own series of cases we have not found it necessary to resort to ventricle puncture before or following drainage of the abscess, but we shall feel free to use it in case it is necessary.

In this group of cases, fortunately for us, localizing signs were definite, and in the majority were not only of cerebellar origin, but were lateralized to the involved

side. For this reason we feel that ventriculography is, in the majority of cases, unnecessary, and should be undertaken only when localizing signs are insufficient to establish the diagnosis. We attempt to avoid even slight alterations of intracranial pressure such as may occur in a brief period during or following ventriculography. It has been our experience that once medullary compression has reached the point at which respiration ceases, there is practically no hope for relieving the condition, even though ventricle puncture is resorted to promptly.

Relative to drainage through a clean or infected field, I, naturally following the concepts of all of the neurosurgeons, believe that drainage should be done through the clean field. I have remarked in this manuscript that drainage may be established through the infected field if definite communication is obtained by the otologist while performing the mastoidectomy. Rarely is such a pathway encountered and for that reason we feel that by far the greater number of such abscesses will, of necessity, be approached through the clean field.

I am glad that Dr. Gotten stressed the point of waiting for signs giving evidence of encapsulation and that he mentioned the fact that cystic serous meningitis must be considered. We, too, have encountered some difficulty in differentiating these two conditions. In one instance a patient with definite history of chronic otitis and mastoiditis presented definite localizing signs of cerebellar involvement in the lobe adjacent to the involved ear. We were happy to have explored for the abscess in this case through a clean field. The exploration was negative and suboccipital craniotomy, which was carried out immediately, permitted exposure and removal of a laterally placed tumor. It would have been extremely unfortunate to have approached this lesion through the infected field.

THE ETIOLOGY OF NERVE DEAFNESS WITH PARTICULAR REFERENCE TO QUININE*

By S. B. Forbes, M.D.
Tampa, Florida

A number of drugs and chemicals have a predilection for the eighth nerve and are capable of causing nerve deafness. They include quinine, the salicylates and alcohol in particular, also tobacco, arsenic, lead, phosphorus, carbon monoxide, carbon disulphide, oil of chenopodium, mercury, morphine and anilin dyes.[1] Of these substances, in all probability quinine causes more deafness than any other. Its most frequent use is in the treatment of malaria, but in addition it is used as an abortifacient, as an oxytocic, and in the treatment of influenza, diseases of the upper and lower respiratory tract, Meniere's disease, corneal lesions, tic douloureux, cardiac diseases and doubtless many other conditions.

*Read in Section on Ophthalmology and Otolaryngology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

As no cinchona bark is produced in the United States, governmental import statistics afford as fair a measure of the consumption of its derivatives as is available, since the records of the large importers and manufacturers of quinine in its various forms are not open to inspection. *Table 1* shows the most recent estimate of the Bureau of Foreign and Domestic Commerce of the Department of Commerce.[2] It is estimated that the cinchona bark imported into this country contains an average of 7 per cent quinine alkaloid. The figures show that the amounts of cinchona bark, quinine sulphate and other quinine, alkaloids and salts from cinchona bark imported annually for the five-year period from 1934 to 1938, inclusive, are fairly stable, although 1937 was the peak year. The prevalence of malaria and the re-export trade with Latin America are influencing factors on the relation of these estimates to actual consumption.

In a talk with Mr. Norman Taylor,[3] Director of Cinchona Products Institute, Inc., of New York, the largest importer of quinine salts in the United States, stated that while he was inclined to think that the consumption of quinine fluctuates widely, depending on the severity of malaria, nevertheless generally speaking perhaps more had been used in the Southern states in the last decade than in the one preceding. Drug companies reported that sales over the last ten years have varied with different types of quinine, the demand for some forms having increased and for others having decreased. The normal consumption of this drug in this country, as estimated in 1934, holds at about 4,700,000 ounces a year.[4] In addition to its usual therapeutic uses, it goes into wine tonics, hair tonics and obscure proprietary remedies marketed successfully in the so-called deep South. The Paris Medicine Company, formerly of Paris, Tennessee, and later of St. Louis, is the largest proprietary consumer of quinine in America, using about 400,000 ounces yearly in the production of its popular product, "E. W. Grove's laxative bromo quinine."[4] After half a century the public continues to keep faith with quinine as an acceptable remedy.

In animal experimentation, Kirstner and Pantchenkoff,[5] after administering quinine orally to rabbits, found the drug in higher concentration in the brain than in any other organ and concluded that it apparently may be taken up not only by the brain but also by the peripheral nerves. Vogt[6] observed that quinine enters the brain substance from the blood more easily than

it enters the cerebrospinal fluid. Experimenting on dogs, Manca[7] demonstrated quinine in the cerebrospinal fluid after intravenous and intramuscular injection and oral ingestion, the highest concentration resulting after intravenous injection.

Numerous investigators have observed the effect of quinine on the auditory apparatus of animals. Administered in massive doses to rabbits, it produced degeneration of the myelin sheath of the auditory nerve in the experiments reported by West,[8] and in therapeutic doses brought about degeneration in the spiral ganglion and peripheral neuron of this nerve. The cytologic constituents of the cells of the stria vascularis and the hair cells showed degenerative changes in the experimental work of Covell.[9] He observed significant changes in the values obtained for the relative vascularity in those animals receiving quinine for several weeks; the vascularity of the stria vascularis increased up to two and a half times that of the control animals in some of the groups. Belemer[10] observed that the resulting distention in the stria vascularis may alter the pressure of the intracochlear fluid.

As pointed out by Wittmaack,[11] there are two ways in which quinine may affect the ear. First, there is the toxic effect of the drug on the nerve cells, particularly the ganglia cells of the cochlea and the associated nerve fibers, a condition that may lead to cochlear degeneration and deafness; and, second, there is labyrinthine hypotonia as a result of a reflex process in the vegetative nervous system. This hypotonic reaction is thought to account for the tinnitus. Strong hypotonic reactions limit the damage to the nerve tissue; weak reactions favor this damage. The action of quinine in conjunction with hypertonia arising from other causes results in a pronounced effect of the poison.

Working with fluorescein and its salts, especially the sodium salt uranin, Benda[12] observed that a somewhat increased permeability of the meninges was indicated in the later weeks of pregnancy and during labor. Mosher[13] demonstrated in experimental animals that quinine fed to the mother or injected caused hemorrhages in the cochlea of the fetus both in the scala vestibuli and semicircular canals and also in the scala tympani. The favorite sites, he noted, for hemorrhage into the mesenchymal tissue of the ear are the mesenchymal tissue surrounding the ossicles, the tissue covering the cochlea, especially at its base, and the mesenchymal tissue lining the bulla cavity.

Quinine may act on the cortical center of hearing, the central nerve paths, the auditory nerve itself or the internal ear, probably on all four. It is established that the spiral ganglion in the human embryo is recognized between the sixth and seventh week and that by the ninth week the cochlear nerve is definitely laid down and has its main characteristics.[14] About this period abortifacients are frequently used, one commonly resorted to being quinine.

During the last decade, first from Southern Rhodesia, then England, India, the Netherlands and, lastly, the United States, have come reports of the administration of from 2½ to 6 grains of quinine daily to expectant mothers during the last several weeks of pregnancy, not at all as an oxytocic, but to insure a normal and easy parturition. The object of the daily divided dosage of the drug is to keep the level of it in the blood as constant as possible. Although unable to explain its action pharmacologically, the authorities of the Cinchona-Instituut of Amsterdam,

QUININE SULPHATE AND CINCHONA IMPORTS INTO UNITED STATES*

	1934		1935		1936		1937		1938	
	Unit	Value	Unit	Value	Unit	Value	Unit	Value	Unit	Value
Cinchona bark, lbs.	1,690,000	$668,000	1,618,000	$631,000	2,051,000	$745,000	1,836,000	$761,000	1,349,000	$588,000
Quinine sulph., ozs.	1,611,000	688,000	1,442,000	646,000	1,565,000	765,000	1,340,000	677,000	977,000	515,000
Other quinine, alkaloids and salts from cinchona bark, ozs.	1,759,000	647,000	2,416,000	415,000	2,180,000	545,000	2,625,000	534,000	1,609,000	370,000

*Latest estimates of the importation of quinine into the United States as published by the Bureau of Foreign and Domestic Commerce of the Department of Commerce.

Table 1

seat of a world monopoly on this product, recently commended this therapy and added:

"The very rare idiosyncrasy to quinine is, when present, evidenced at once and then one can either try another quinine salt or stop the administration."[15]

Perhaps so with the mother, but the question arises as to the possible effect on the fetus of a constant level of quinine, even though small, in the maternal circulation during the last several weeks of intra-uterine life.

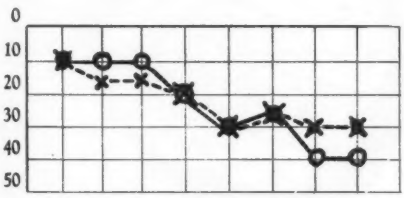
Certainly Taylor[1] has supplied ample clinical evidence to show that quinine administered to the mother during pregnancy to induce labor, as an abortifacient or in the treatment of concurrent disease may cause deafness in the newborn. The impairment of hearing acquired *in utero* may manifest itself merely as a diminution in the function of hearing and not necessarily as complete deafness. With adults, the amount of the drug required to produce unfavorable aural effects varies widely; likewise, doubtless, the quantity in the maternal circulation capable of damaging the delicate aural mechanism of the fetus is also widely variable.

Four cases of so-called congenital deafness have come under my observation in children ranging in age from 20 months to 5½ years. In two of these cases the mothers had been given quinine continuously for several weeks in the treatment of malaria during the period of pregnancy. Aural examination of these patients, aged 20 and 34 months, revealed no evidence of malformation; the drums and light reflexes were normal as were also the caloric tests. In neither was there an aural palpebral reflex present in response to a loud noise, nor on striking a tuning fork close to the head. There was no evidence whatsoever of hearing. The Wassermann reaction was negative both for the parents and the child in each instance. Neither child had been delivered by forceps nor was there any apparent injury at birth.

In the third and fourth cases the children had both impaired hearing and amblyopia with the optic symptoms overshadowing the aural.

The mother in the third case, having been secretly married, had taken quinine as an abortifacient for two months after first missing her menstrual period. She had had nausea and vertigo frequently during this time and constant tinnitus and deafness, symptoms that disappeared as soon as she discontinued taking the quinine. The delivery was normal, no instruments being used. The child, a boy, was 37 months old when his parents brought him for examination, stating that he always held objects very close to his eyes, bumped into things and did not hear well. The child was highly nervous and had a pronounced fixation nystagmus. His vision was very limited, for he could discern only large objects in bright illumination. No refractive error could be made out. Examination of the eyegrounds showed intense pallor of the discs with loss of detail and small retinal vessels. Aural examination, including the caloric tests, was negative. There was definite impairment of hearing, but to what degree was difficult to ascertain. Serologic findings both for the mother and the child showed only negative results. The pediatrician who referred the patient felt that the child was normal in every other way.

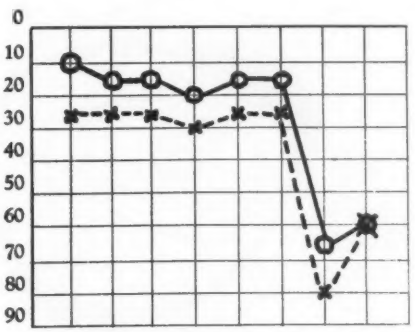
The fourth case was that of a boy, aged 5½ when first examined. Telling the mother that labor should be induced because she was ten days overdue, the attending physician had repeatedly given her quinine at hourly intervals during the last twenty-four hours prior to confinement. In consequence, she had suffered from tinnitus and such extreme vertigo that she could hardly stand. The delivery next day was normal. She stated that the child at an early age had begun to hold objects close to his eyes and to look sideways or out of the top



Audiogram of E.B.B. (age 8) male. Date 10/21/39
Hearing loss, A.D. = 20.00 % = O
A.S. = 20.00 % = X

Fig. 1

E.B.B., a boy, aged 8, whose mother was given quinine to induce labor at the time of his birth, early gave evidence of impaired hearing and amblyopia, which was confirmed by examination when he was five and one-half years of age. Audiogram recently made shows present impairment of hearing. Vision has improved.



Audiogram of E.S. (age 21) male. Date 9/23/39
Hearing loss, A.D. = 13.28 % = O
A.S. = 21.28 % = X

Fig. 2

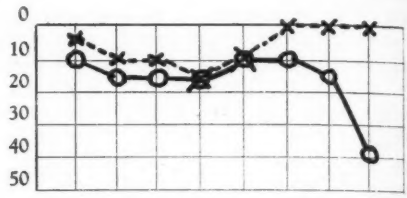
Audiogram shows defective hearing in E.S., a young man, aged 21, who had suffered a considerable loss of hearing and vision after having been given massive doses of quinine when eight and one-half years old.

of the eyes. She had soon noticed, too, that his hearing was defective. On examination, the patient had a very noticeable fixation nystagmus; the vision was 20/50 in the right eye and 20/50 minus in the left eye. There was pallor of the nerve heads, but no vascular change. A low-grade hyperopic astigmatic error was present. The results of the aural examination were negative as were the caloric tests. Audiograms made at that time were not satisfactory, but they showed loss of hearing, particularly for the higher tones. Recently, after two and a half years, the patient was again examined. Vision had improved to 20/30 in each eye, and the nerve heads showed more color. This improvement would seem to indicate that the original damage to the eye was not severe enough to remain wholly permanent. The definite nerve deafness that is now present is indicated in the audiogram shown in *Fig. 1.*

In 1936, Richardson[16] reported two cases, one of amaurosis and one of amblyopia, in children in which the etiologic factor appeared to be quinine given the mother during pregnancy. In one of these instances the quinine had been given for malaria and in the other to induce labor. Taylor[1] previously had reported several cases of deafness in children apparently of like origin. If otologists and ophthalmologists were on the alert for such cases and would undertake the delicate and difficult task of eliciting the facts behind them, many more could no doubt be brought to light.

An audiogram and chart of the visual fields in a case in which amblyopia and deafness were both present are shown in *Figs. 2* and *3*. In this case a young man, aged 21 years when examined, had been given massive doses of quinine when 8½ years old. Thereafter his vision and hearing had both failed very perceptibly. Aural examination gave negative results; the vestibular tests were normal. The vision was 20/100 in each eye and was not improved by glasses. The eyegrounds showed pallor of the nerve heads and the retinal vessels were small. There was a pronounced fixation nystagmus. The Wassermann reaction was negative, and there were no other significant findings.

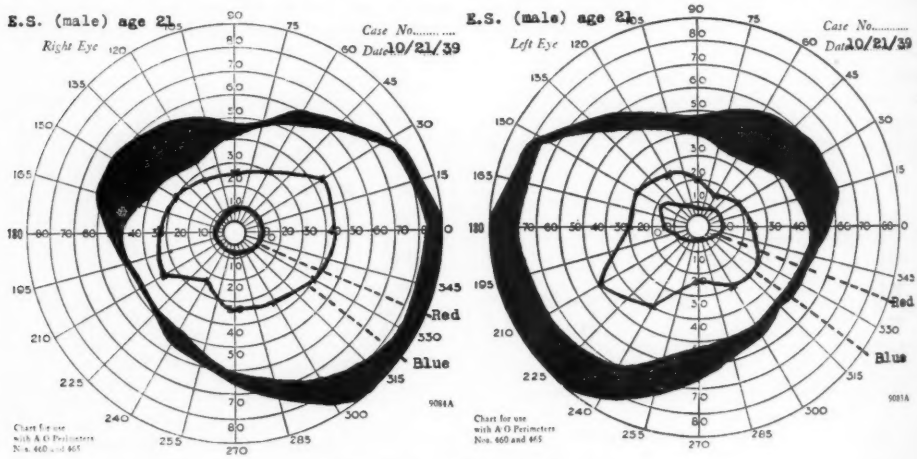
From our records 1,218 cases of all types of deafness were reviewed, and out of this number 274 cases representing only pure nerve deafness and 944 cases of all other types of deafness were selected. The histories in these two groups of cases were carefully studied, questionnaires were sent to patients in instances where addi-



Audiogram of E.A.D. (age 63) male. Date 11/7/39
Hearing loss, A.D. = 9.28 % = O
A.S. = 6.64 % = X

Fig. 4

E.A.D., a man, aged 63, complained of tinnitus in the right ear of several months' duration. Over a long period he had been taking quinidine in the treatment of a mild cardiac condition. Neither on examination nor in the history of this patient were there other findings of possible etiologic significance. The audiogram shows a loss of hearing in the right ear for the highest tone.



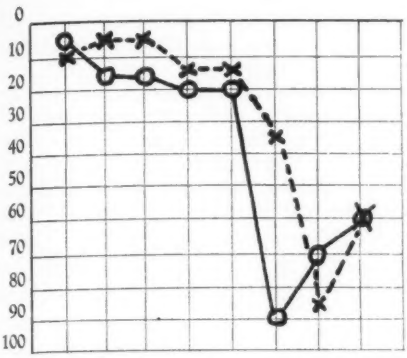
Five mm. discs at distance of twelve inches.

Fig. 3

Charts show visual fields of E.S., the young man whose audiogram is shown in *Fig. 2*. Examination of the eyes revealed the characteristic changes that may occur following quinine therapy. Vision was 20/100 in each eye and was not improved by glasses.

tional data were desirable, and some patients were interviewed personally in the interest of the survey. It transpired that 234 histories of cases of nerve deafness and 832 histories of cases of all other types of deafness could be satisfactorily analyzed. In the first group, in 92 of the 234, or 39.3 per cent, there was a definite history of the ingestion of quinine over a considerable period of time. Eighteen of these patients, or 7.6 per cent, gave as their personal opinion that quinine had caused their deafness, and five, or 2.1 per cent of the total number, stated that a single course of quinine therapy, in which the drug had been ingested in large doses, had resulted in sudden and permanent impairment of hearing.

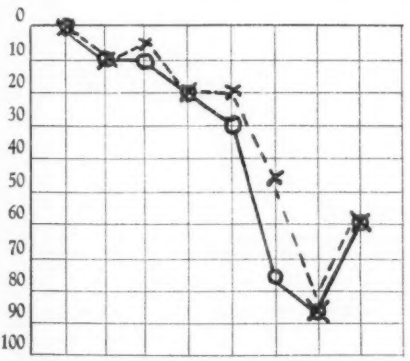
In the second group, 82 of the 832 histories of cases of deafness other than nerve deafness, or only 9.8 per cent, showed that these patients had taken quinine, and none of the 82 associated



Audiogram of H.E.B. (age 56) male. Date 2/20/24
Hearing loss, A.D. = 34.64 % = O
A.S. = 17.28 % = X

Fig. 5-a

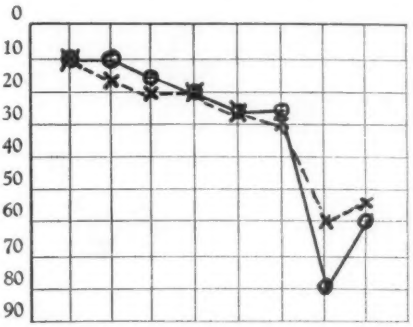
H.E.B., a white man, aged 71, had repeated attacks of malaria, including blackwater fever, over a period of many years spent in Africa as a missionary. The very frequent ingestion of large doses of quinine during that time was always followed by tinnitus and deafness. Two audiograms are shown. The first one was made in 1924.



Audiogram of H.E.B. (age 71) male. Date 9/20/39
Hearing loss, A.D. = 33.28 % = O
A.S. = 22.64 % = X

Fig. 5-b

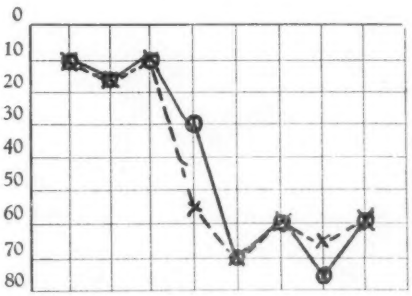
The second audiogram was made in 1939, and in the fifteen-year interim no quinine had been taken. Despite the age of the patient, there was no real progression in the deafness.



Audiogram of H.P.B. (age 52) male. Date 8/24/38
Hearing loss, A.D. = 18.64 % = O
A.S. = 20.00 % = X

Fig. 6

H.P.B., a male physician, aged 52, had from early childhood been accustomed to take quinine for colds, influenza and many attacks of malaria. He used tobacco moderately, alcohol not at all, had had no ear trouble in childhood or adult life, and had no history of familial deafness. He definitely attributed his deafness to quinine. Audiogram shows the measure of impairment, particularly for the high tones.

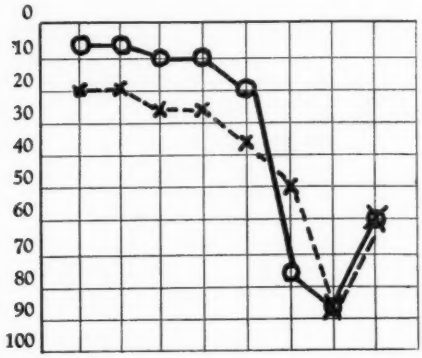


Audiogram of M. F. (age 18) female. Date 11/30/38
Hearing loss, A.D. = 42.64 % = O
A.S. = 49.28 % = X

Fig. 7

M. F., a girl, aged 18, had a history of deafness since beginning school. Numbers of times during childhood she had been given quinine, but for four years prior to examination, on the advice of her physician, she had taken none. During that period the deafness had not seemed to progress. There was no history of nose or throat trouble, abscessed ears or familial deafness. Examination of the ears, nose, throat and blood gave negative results. The vestibular tests were normal. Audiogram shows the degree of defective hearing.

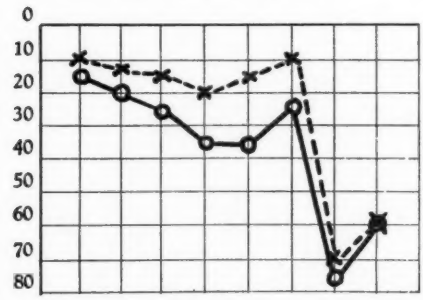
the taking of quinine with their deafness. That quinine was a factor to be considered in 39.3 per cent of the cases in the first group and in but 9.8 per cent of those in the second group seems both striking and significant, especially so since the second group was three and a half times larger than the first.



Audiogram of O.D.L. (age 47) male. Date 10/14/39
Hearing loss, A.D. = 28.00 % = O
A.S. = 29.28 % = X

Fig. 8

O.D.L., a man, aged 47, had in early adult life taken 40 grains of quinine daily in ten-grain doses for six days. Tinnitus and almost total deafness persisted during and for some time after this therapy. For one year thereafter the hearing improved, but never returned to normal. There was no history of familial deafness nor of the use of alcohol or tobacco. Examination of the ears, nose and throat gave negative results, as did the Wassermann test. Vestibular tests showed a marked hypo-irritability in the left ear.

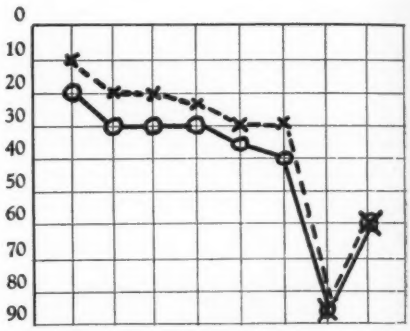


Audiogram of P.B. (age 57) female. Date 3/1/39
Hearing loss, A.D. = 25.28 % = O
A.S. = 12.00 % = X

Fig. 9

P.B., a woman, aged 57, had taken 500 grains of quinine in less than two weeks, one and a half years prior to examination. During and after the treatment she had experienced vertigo, some nausea and pronounced tinnitus. For a period of two months the initial loss of hearing decreased somewhat, but marked buzzing in the right ear persisted. There was no history of familial deafness, and examination of the ears, nose, throat and blood was essentially negative. The eustachian tubes were patent.

Quinidine also is now coming to the attention of otologists as a possible cause of aural symptoms. This drug is described as slightly more toxic, perhaps, than quinine and fully as potent as an antimalarial. Although it is used comparatively rarely for this purpose, many patients who have an idiosyncrasy to quinine are able to tolerate it. Its most important and extensive use is in the management of certain forms of irregularity of the heart, especially auricular fibrillation. In many instances, however, unpleasant symptoms such as headache, increased palpitation, precordial pain, nausea or vomiting and ringing in the ears have interrupted the treatment. Recently there came under my observation a patient, aged 63 years, who had taken quinidine almost daily in nine-grain doses since January, 1938. He complained of a buzzing sound in the right ear that had annoyed him for several months. He used neither alcohol nor tobacco and had no history of familial deafness. Examination was essentially negative. The audiogram shown in *Fig. 4* indicates a decided lowering of perception for the highest tone in the



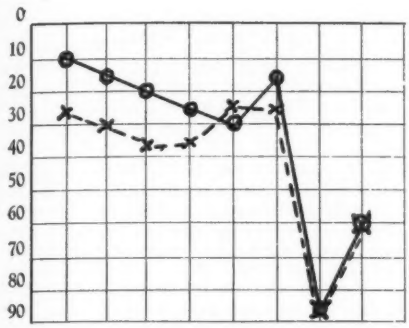
Audiogram of M.H.N. (age 62) male. Date 11/1/39
Hearing loss, A.D. = 28.00 % = O
A.S. = 22.64 % = X

Fig. 10

M.H.N., aged 62, was one of three brothers in a family of six children. All three brothers and one sister had had an appreciable degree of deafness since early childhood. Throughout childhood they had been given again and again in the treatment of malaria five grains of quinine every four hours continuously until 60 grains had been taken, and in addition plasters of quinine in oil had been applied to the chest. This therapy was repeated every seventh day for at least six weeks. After the forty-second day it was discontinued if there had been no recurrence of chills. The ingestion of quinine was always accompanied by vertigo and tinnitus. The two unaffected sisters apparently had a high tolerance for the drug. The mother became deaf at the age of 60, too late in life to be suggestive of otosclerosis, as there was no noticeable early loss of hearing in this mother of six children. The patient's deafness had increased greatly during the four years immediately preceding examination, which revealed no significant findings. The patient used tobacco moderately, but no alcohol.

right ear. In this case the etiologic role of quinidine is suggestive.

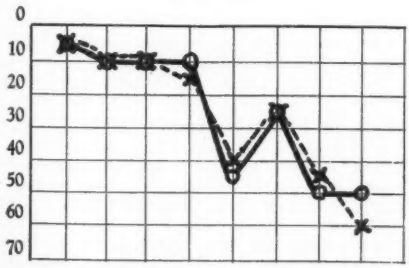
The audiograms presented in *Figs. 5* to *13*, inclusive, illustrate further the rather spectacular results that are in some cases apparently due to the ingestion of quinine. However, in an evaluation of the role of this drug as an etiologic factor in nerve deafness the fallibility of patients, especially when reciting their ills, is to be considered. The onset of this type of deafness is insidious, for the high tones are first affected and are not readily missed, since they are above the conversational tones. Also, age is a factor that complicates the picture in adult deafness because of the diminution of perception for the high tones as age advances. Nevertheless, in the study of the etiology of nerve deafness quinine may well be a major consideration of the otologist.



Audiogram of J.E.B. (age 48) male. Date 7/16/39
Hearing loss, A.D. = 18.64 % = O
A.S. = 22.64 % = X

Fig. 11

J.E.B., aged 48, had experienced deafness and tinnitus for two years, during the first of which he had taken repeated doses of bromoquinine for nervousness, insomnia, chills and fever. There was no history of familial deafness, and examination of the ears, nose, throat and blood gave negative results.



Audiogram of A.T.H. (age 54) male. Date 8/23/35
Hearing loss, A.D. = 21.28 % = O
A.S. = 21.28 % = X

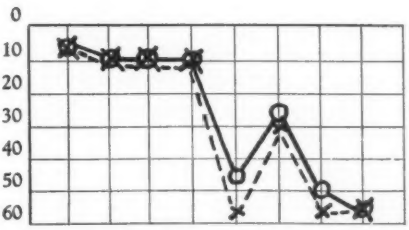
Fig. 12-a

A.T.H., aged 58, had suffered from impaired hearing for ten years. The onset of the deafness was coincident with the taking repeatedly of as much as 60 grains of quinine in twenty-four hours in the treatment of malaria. Prostration, vertigo and tinnitus accompanied this therapy. Examination of the ears, nose and throat revealed nothing of importance, nor was there a history of familial deafness. Two audiograms are shown. The first one was made in 1935

CONCLUSIONS

Information from all available sources indicates that the consumption of quinine has been as great in the decade immediately past as in the one preceding.

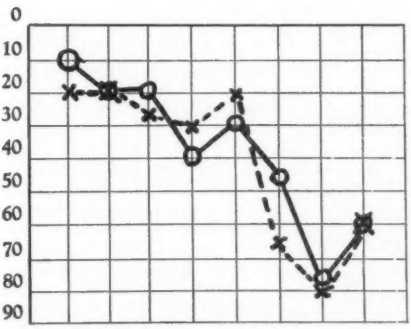
It is well established that this drug has an affinity for the auditory nerve.



Audiogram of A.T.H. (age 58) male. Date 5/15/39
Hearing loss, A.D. = 21.28 % = O
A.S. = 25.28 % = X

Fig. 12-b

The second audiogram was made in 1939. In the interim the patient took no quinine. Progression of the deafness has been slight.



Audiogram of C.F.C. (age 39) male. Date 10/2/39
Hearing loss, A.D. = 30.64 % = O
A.S. = 30.64 % = X

Fig. 13

C.F.C., aged 39, had as a boy of 17 suffered impairment of hearing following the taking of quinine over a period of six months in the treatment of malaria. There had been no change in the condition until the ears became stopped up and painful prior to examination. A mycotic infection of both external auditory canals yielded promptly to treatment. Otherwise, there were no significant findings, nor was there a history of familial deafness.

There is evidence, both experimental and clinical, to support the view that quinine administered to the mother during pregnancy may cause deafness, and also amblyopia, in the child.

Apparently in some instances it may cause both impairment of hearing and of vision that may be permanent when administered in large doses to a child.

In a series of 234 cases of nerve deafness and 832 cases of deafness other than nerve deafness, the percentage of patients who had a history of having taken quinine was four times greater among those with nerve deafness. An appreciable number of those having nerve deafness attributed the impairment of hearing to the ingestion of quinine, but none of the small number who had taken the drug among the much larger group that had other types of deafness, associated the condition with quinine.

A series of audiograms illustrates the suggestive role of quinine as an etiologic factor of nerve deafness.

REFERENCES

1. Taylor, H. Marshall: Nerve Deafness of Known Pathology or Etiology: Deafness from Drugs and Chemical Poisons. Laryngoscope, **47**:692-705 (Sept.) 1937. Cited in the 1937 Year Book of the Eye, Ear, Nose and Throat, p. 340.
   Does Quinine as Used in the Induction of Labor Injure the Ear of the Fetus? Jour. Fla. Med. Assn., **20**:20-23 (July) 1933.
   Prenatal Medication as a Possible Etiologic Factor of Deafness in the New Born. Arch. Otolaryng., **20**:790-799 (Dec.) 1934.
   Further Observations on Prenatal Medication as a Possible Etiologic Factor of Deafness in the New Born. Sou. Med. Jour., **28**:125-130 (Feb.) 1935.
   Prenatal Medication and Its Relation to the Fetal Ear. Surg., Gyn. & Obst., **64**:542-545 (Feb.) 1937.
2. World Trade Notes on Chemical and Allied Products, Chemical Division, Bureau of Foreign and Domestic Commerce, Department of Commerce, **13**:318 (May 13) 1939.
3. Personal communication to the author, dated Sept. 25, 1939.
4. Cinchona-Quinine to You. Fortune, p. 76 (Feb.) 1934.
5. Kirstner, A. A.; and Pantchenkoff, M. M.: Distribution of Quinine in the Organism. Klin. med. (No. 17) **9**:751-758, 1931.
6. Vogt, M.: Distribution of Medicaments in Various Regions of the Central Nervous System and Their Microdetermination in Tissue. Arch. f. exper. Path. u. Pharmakol., **178**:560-576, 1935.
7. Manca, S.: Permeability of the Central Nervous Barrier to Quinine: Experimental Study. Riv. di Malariol. (seg. 1), **13**:601-608, 1934.
8. West, Ray A.: Effect of Quinine upon the Auditory Nerve. Amer. Jour. Obst. & Gyn., **36**:241-248 (Aug.) 1938.
9. Covell, W. P.: A Cytologic Study of the Effects of Drugs on the Cochlea. Arch. Otolaryngol., **23**:633-641 (June) 1936.
   Effects of Drugs on the Stria Vascularis. Arch. Otolaryngol., **27**:438-443 (April) 1938.
10. Belemer, J. J.: Vessels of the Stria Vascularis with Special Reference to Their Function. Arch. Otolaryngol., **23**:93-97 (Jan.) 1936.
11. Wittmaack, K.: Ueber Chinin wirkung im Gehoerorgan. Ztschr. f. Hals-, Nasen- u. Ohrenh., **39**:211-222 (Jan.) 1936.
12. Benda, Robert: Influence of Menstruation and Pregnancy on the Permeability of the Meninges. Munchen. med. Wchnschr., **72**:1686-1688 (Oct. 2) 1925; abstracted in J.A.M.A., **85**:1681 (Nov. 21) 1925.
13. Mosher, Harris P.: Does Animal Experimentation Show Similar Changes in the Ear of the Mother and the Fetus After Ingestion of Quinine by the Mother? Laryngoscope, **48**: 361-395 (June) 1938.
14. Personal communication from Dr. G. L. Streeter, of the Department of Embryology of the Carnegie Institution of Washington, cited by Taylor, H. Marshall: Nerve Deafness of Known Pathology or Etiology: Deafness from Drugs and Chemical Poisons. Laryngoscope, **47**:692-705 (Sept.) 1937.
15. Cinchona-Instituut: The Use of Quinine to Insure a Normal and Easy Parturition, Amsterdam, 1938. Cites Hewetson, W. M.: Brit. Med. Jour. (Jan. 28) 1928; Mitchell, D. A.: The Use of Quinine in Normal Labor. Brit. Med. Jour., **1**:144-146 (Jan. 25) 1930 (400 Cases); Ganner, P. J.: Results of Ante-natal Administration of Quinine. Brit. Med. Jour., **2**:205-6 (Aug. 3) 1935 (50 Cases of Normal Primiparae); Green-Armytage, V. B.: Brit. Med. Jour., p. 397 (Aug. 26) 1933; Smit, H. P. A.: Ned. Tydschr. v. Geneesk., p. 5303 (Nov. 28) 1936. Smith, Linton: Ante-natal Administration of Quinine. Jour. Med. Assn. Ga., **25**:247-250 (July) 1936 (60 Cases).
16. Richardson, Shaler: The Toxic Effect of Quinine on the Eye. Sou. Med. Jour., **29**:1156-1164 (Dec.) 1936.

409 Citizens Building

DISCUSSION (*Abstract*)

Dr. John H. Foster, Houston, Tex.—I have been a victim of nerve deafness which resulted from the administration of quinine when I was a child. This fact had something to do with my becoming interested in otology.

When I began to practice in Houston thirty-three years ago, a large per cent of the adults whom I saw had in the past lived in malarial districts and had taken a great deal of quinine. I made a practice of testing their hearing and found that practically all of them had some degree of nerve deafness, frequently quite marked. I came to the conclusion, therefore, that practically all persons who had taken large quantities of quinine over a period of years had some degree of nerve deafness, frequently not enough, of course, to be noticed by the patient, but a test showed impairment of the high notes to a considerable degree.

In recent years, malaria has been largely eradicated and this condition does not prevail. Then, too, a very important point, quinine today is not administered in the enormous doses formerly used in our country. When I was a boy in the country we kept quinine on hand in malarial districts, and dished it out by the teaspoonful in coffee, and we took it every day, took a spoonful in a cup of black coffee as a routine measure.

I have always been under the impression that the injury is produced primarily by congestion rather than by direct effect upon the nerves. In the few cases of amblyopia from quinine that I have seen, there was enormous engorgement of the vessels of the fundus, with hemorrhages.

I should like to call attention to another drug that is sometimes a factor in nerve deafness, namely, tobacco. That tobacco does affect the internal ear is evidenced by the infection of the middle ear in novices in its use. Some time ago I saw a young man referred by another otologist simply because he could find no cause for a rather sudden and marked loss of hearing. The only clue I could elicit was the excessive use of tobacco. He gave up smoking and in three weeks' time he showed an improvement of one-third in his hearing. A return to smoking some months later resulted in the same loss of hearing as when he was first seen.

It must not be inferred that I believe that all users of quinine or tobacco do or will become deaf. Unquestionably an idiosyncrasy to the drug is an important factor, and in giving quinine, for instance, if one finds

that a patient quickly shows ear symptoms, the drug should be discontinued or used very cautiously.

Dr. Charles D. Blassingame, Memphis, Tenn.—Early in life I had malaria and took a great deal of quinine and it made me very deaf for the time being.

The implication of the effect of quinine, since we do accept the fact that quinine causes deafness, is, I think, very great. Otologists are in a unique position in this instance in being able to see definitely that nerve involvement is directly due to a specific agent. That means to us quinine is not the only thing that may give the same effect.

If quinine and other substances (and Dr. Forbes has brought out that many other substances do also) affect the auditory nerve, what about the problem of toxic substances in the body as a result of infection?

That prepares us to accept the specific effect of toxin from infection. It also prepares us to accept the variability of the effect of toxins in the system.

Deafness is not the only deleterious effect of quinine. It tends to cause blindness, as Dr. Forbes has brought out. Idiosyncrasy of the person taking the substance has something to do with it, as with other toxins.

At the Academy meeting, during a symposium on hypertension, I was very much struck with the fact that focal infection was not mentioned as a direct or remote factor in hypertension. Of course, we do not know that infection causes hypertension, but we do know that internists always have foci of infection removed in trying to get at the cause of hypertension.

The implications of the effect of quinine on the auditory nerve are wide.

Dr. Albert L. Bass, Louisville, Ky.—I should like to ask Dr. Forbes how much of a dose can be given to a patient without harm, maintaining a constant level in the blood, and what is the dose of quinine absorbed in the system normally. I realize the variability and idiosyncrasy of the individual. I have heard it estimated that six grains of quinine is as much as the system absorbs in twenty-four hours and that any excess is superfluous.

Dr. Murdock S. Equen, Atlanta, Ga.—Dr. Linton Smith, of Atlanta, recently presented before the Fulton County Medical Society a series of six hundred cases in which he had used quinine dihydrochloride, one and one-half grains three times a day, over a period of three weeks prior to the expected delivery. His observations have been that by so doing the muscular action of the uterus is increased, thereby shortening the period of labor and lessening the pain. Dr. Smith's opinion was that deafness had resulted from the use of massive doses of quinine and did not follow when small amounts were given. He has used this drug since 1933 and has never observed any cases of deafness following its use.

Dr. Forbes' paper is of particular interest to those living in a malarial section; however, since travel today is extensive, the mode of transportation rapid and the whole world closely knitted together, no disease can be termed endemic.

Dr. C. C. Cody, Houston, Tex.—The question of dosage and age of children is an important one. Repeatedly have I observed that doses of a proprietary quinine preparation formerly given for colds and a wide variety of diseases among children, in which there are two grains to the teaspoonful, given for one to two days, would bring to the otologist a noticeable amount of impaired hearing.

Children vary a great deal in their sensitiveness to quinine and also to aspirin. It has been my observation that following aspirin in large doses for children under 7 or 8 years of age, five grains every two hours, five grains every four hours, quite frequently there is a noticeable impairment of hearing.

I think the otologists would do a great deal if they would call attention of the pediatricians and general practitioners to the wide variety of drugs and the relatively small doses in some individuals which may produce impaired hearing. Quinine and aspirin are not innocuous drugs.

Dr. Forbes (closing).—The effect of quinine on the mechanism of the eye is of course comparable to its effect on the auditory apparatus, both being apparently the result of toxicity and ischemia. Dr. Foster's description of an acute amaurosis from quinine with engorged retinal vessels and hemorrhages is of particular interest to me, for I have never observed an acute case of poisoning caused by quinine. The usual syndrome, as described in the literature, is that of retinal anemia with contracted vessels and even at times a cherry-red spot in the macula, comparable to an embolus of the central artery. The nerve fiber and ganglion cell layer of the retina is affected by the drug and perhaps the inner nuclear layer. Some authors have concluded that it damages the rods also, as the peripheral vision is involved.

In the ear, quinine damages the spiral ganglion cells and the auditory nerve, produces vascular changes, as I have said, and particularly affects the basal coil of the cochlea and the external hair cells.

Tolerance for quinine evidently varies greatly with the individual. I showed you the audiogram of a patient who was one of six children, four of whom were deaf while two had normal hearing; yet all had taken enormous quantities of quinine over long periods of time.

Fluctuation in the sale of quinine has in recent years been due in part to the inroads made by the excellent program promoting "atabrine." However, the experiences of individual practitioners with this newer drug have turned many of them back to quinine with consequent recovery in the demand for this product. Its increasing use in various forms, as, for example, quinidine, should make the otologist and the ophthalmologist alert to possible damage to the ear and the eye from this source.

Only two weeks ago an obstetrician told me that he was really frightened a few days before when a patient, three weeks after delivery of her baby, said to him that she believed the child was deaf. He had given the mother a considerable amount of quinine during the twenty-four hours immediately preceding delivery. He assured me he would never administer this drug again to the pregnant patient. We may well profit by his experience and example and advise our colleagues, particularly those in obstetrics, to do likewise. By so doing we may prevent some cases of so-called congenital deafness.

PRIMARY CUTANEOUS GILCHRIST'S DISEASE*

By J. LAMAR CALLAWAY, M.D.
and
VINCE MOSELEY, M.D.
Durham, North Carolina

This paper is intended as a brief discussion of the primary cutaneous form of Gilchrist's disease or North American blastomycosis.[1,2]

This disease was first described by Gilchrist[1] in June of 1894. A description and study of the organism causing it was published by Gilchrist and Stokes[3] in 1896. Shortly after Gilchrist first described this entity a patient with somewhat similar clinical findings was described by Buschke and Busse in Germany. In the years following, many similar patients have been reported in the medical literature, nearly all of which have been roughly grouped as cases of blastomycosis in spite of the fact that apparently a great variety of fungi have been implicated as the etiologic agents. The name, blastomycosis, has come to embrace a large variety of fungous diseases as found in Europe and South America as well as in the North American continent. Much of this confusion has arisen because of the tendency to classify many types of lesions as blastomycosis if, upon pathologic examination, yeast-like or budding fungi are found in the tissues so examined. The use of the name Gilchrist's disease will do much to obviate the confusion existing at present. We agree with Redaelli and Cifferri[4] that by definition this name must be reserved for those cases caused by *Blastomyces dermatitidis*. This is the name originally given the organism by Gilchrist and Stokes[6] in their studies reported in 1898.

Since 1898, at least nineteen names have been applied to the fungi isolated from cases of North American blastomycosis.[7] Studies which have recently been made in the laboratories of Duke Hospital by Martin[10] and Conant[5] tend to show, however, that in their serologic reactions and morphologic characteristics these strains are really all one and the same organism. It is, therefore, proposed by Conant[5] that for the present the name *Blastomyces dermatitidis* be used to designate the etiologic agent of Gilchrist's disease.

Some clarification of the confusion existing in regard to the etiologic agents responsible for the production of the various types of European and South American blastomycosis has been accomplished.[1,8,9] With these advances a less confusing nomenclature has resulted and it is to be hoped that concomitant therapeutic advances may be effected.

INCIDENCE AND GEOGRAPHIC DISTRIBUTION

Because of the writings in dermatologic texts and other reports, it is thought by many that Gilchrist's disease is confined almost entirely to that region known as the middle western United States. Although Gilchrist's disease is essentially a disease of the North American continent, it must be realized that it is apparently more widely distributed than has been thought by some authors. There are case reports of this disease from at least twenty-eight states, in regions that are so widely separated as California, New York and Texas.[7]

The disease seems to have its onset more often in the summer months. As with many other diseases, those in the lower economic brackets are apparently more frequently infected.

Males are seemingly infected about five times as often as females. Of one hundred and sixty-six reported cases of cutaneous Gilchrist's disease, one hundred and thirty-five males were infected and thirty-one females.[7] The infection has been reported in all age groups.[7]

The source of infection is apparently not known at present. Damp moldy wood has been suspected of harboring the fungus.[13] Direct infection from man to man except as by an accident such as may occur at the autopsy table must be quite rare. We could find no case reports of such transference of the infection except as in the accidental inoculation at postmortems.

DIAGNOSIS

There are clinically two forms of Gilchrist's disease: first, the primary cutaneous form which is the result of the inoculation of the organism *Blastomyces dermatitidis* into the skin. The second form is that in which there is a systemic infection of the body by this organism and secondary cutaneous involvement occurs with lesions produced in a manner similar to that seen in cases of secondary cutaneous tuberculosis. In this paper we are concerned only with the primary cutaneous form.

---

*Read in Section on Dermatology and Syphilology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

*From the Section of Dermatology and Syphilology of the Department of Medicine, Duke University School of Medicine

The diagnosis of this disease rests on the history, clinical appearance of the lesions, and laboratory tests.

The history is usually that of a slowly progressive skin lesion. Little pain or discomfort is experienced and constitutional symptoms are absent. This is of importance in contrast with the secondary type of cutaneous involvement where the constitutional symptoms are frequently quite marked, and definite symptoms in reference to systems or organs other than the skin are often the primary complaints with multiple skin lesions and sinus tracts as secondary complaints.

The gross appearance of the skin lesions is of great diagnostic importance, and careful inspection must be made.

There are clinically two types of primary cutaneous Gilchrist's disease. The first results from the rather superficial inoculation of the organisms into the skin. This might be termed the "papulo-verrucous type." The second or so-called "gummatous" or "nodular type" is the result of the inoculation of the organisms deep into the corium.

The "papulo-verrucous type" begins as a papule or papulo-pustule in the superficial layer of the skin. This lesion breaks down and discharges a purulent or sanguino-purulent material in which the organisms may be found. The lesion may crust over, but crusting is not a prominent sign. Slowly the lesion spreads by peripheral extension due to auto-inoculation of adjacent skin areas. The contour of the lesions often assumes serpiginous or arciform shapes because of this mode of spread.

The more central parts of the spreading lesion undergo spontaneous healing with scar formation. Contracture from the scar is usually very slight.

The margins deserve careful inspection, because these often have the most clinical diagnostic significance. They are heaped up and assume a quite distinctive delicate papilliform or fine verrucous character. The fine verrucous appearance is to be especially noticed as in contrast with the coarser verrucous appearance of verrucous tuberculosis cutis or that shown by some epitheliomas. It is also to be noticed that the downward slope of the margins is quite abrupt. A characteristic dusky violaceous hue is present at the most peripheral portion. In this erythematous zone small miliary-like abscesses will be found.

The nodular or gummatous type of lesion starts from infection rather deep in the corium. It begins as a deep-seated, rather soft, subcutaneous nodule. The skin overlying the nodule often has a dusky erythematous hue. These nodules may vary in size from one-half to three centimeters in diameter or larger. The centers of these nodules soften and break down. Sanguino-purulent material is discharged and ulceration results. At first there is nothing to be seen clinically of diagnostic importance. Soon, however, the peripheral margins begin to show the characteristic signs to be sought for, namely, heaped up margins of a fine verrucous type with an abrupt peripheral slope, a zone of dusky violaceous erythema, and miliary abscesses. The lesions tend to be single or to occupy a single skin area. They are found most often on the exposed body areas.

At Duke Hospital we have seen nine cases of proven primary cutaneous Gilchrist's disease. Seven of the patients were males and two were females. Six were colored and three were white. All were from rural areas. Their ages ranged from 16 to 73 years. All but two were over 30. In this group of cases we found the lower leg to be involved in four, the cheek in two, the hand in two, the lip in one, the forehead in one, the upper arm in one, the chest wall in one, and the buttocks in one. Four of the cases had more than one area of skin involved with primary lesions, as for example, in patient M. W. (Hospital No. 67413), a 63-year-old white man, who had primary lesions on the right upper arm and on the forehead.

Verrucous tuberculosis cutis, bromoderma, iododerma, epitheliomas, syphilitic gummas, and cutaneous fungus diseases of etiology other than *Blastomyces dermatitidis* may prove difficult to differentiate clinically from cutaneous Gilchrist's disease and here various laboratory methods will have to be called on as aids in diagnosis.

There are five important laboratory diagnostic aids.

The first method is that of the examination of freshly prepared smears of material obtained from the abscesses or purulent discharges. A drop of pus is placed on a slide to which is added a few drops of 15 per cent aqueous potassium hydroxide solution in order to dissolve away the leukocytes and cellular debris present. A cover slip is then placed over this material and examination is made with the high dry or oil immersion lens of a microscope. The organism of the *Blastomyces dermatitidis* will appear as doubly

contoured spherical single or budding bodies eight to twenty-three microns in size.

The second method is that of the recovery of the organism by culture. This is the most exact diagnostic method of all. Cultures[7] are made by streaking rather heavily the purulent material obtained from the lesions onto blood agar plates and Sabouraud's slants. From two to three weeks are often required for the organisms to grow out. Therefore, no cultures should be discarded until they have been observed for at least three weeks. The blood agar plates are incubated at a temperature of thirty-seven degrees Centigrade. Colonies of the organism appear as small wrinkled waxy growths. Microscopic examination of these will reveal spherical or rounded thick wall cells, many of which will show budding while others will have rudimentary hyphae.[7]

Sabouraud's slants are incubated at room temperature. Of the two types of media used for culture purposes, on this will occur the most luxuriant growth. The colonies appear as large whitish mold-like growths with aerial mycelium. With age the colonies become brown. Microscopic study of these colonies will show numerous branched hyphae with lateral conidia and thickly swollen chlamydospores.[7]

The third laboratory aid consists of skin testing the suspected patient with an intracutaneous test dose consisting of one-tenth of a cubic centimeter of a standard heat killed vaccine. This test may be considered quite analogous to the tuberculin skin test and the results are read similarly.

As a fourth laboratory aid we have also used a complement fixation test with some degree of success.[10] This test will probably seldom have to be called on in cases of primary cutaneous Gilchrist's disease.

The fifth method is that of biopsy and pathologic study. The histopathology of cutaneous Gilchrist's disease is quite distinctive. Epidermal hyperplasia of an extreme degree is found. Difficulty is often experienced in distinguishing this hyperplasia from the quite similar hyperplastic changes seen in epitheliomas. In the epidermal layer the intra-epidermal miliary abscesses are seen in which the organisms can be frequently distinguished. Suppurative and tubercle-like reactions are found in adjacent areas of the skin section. In the deeper parts of the corium tubercles with mononuclear cell infiltration and giant cell formation occur. The bodies of the *Blastomyces dermatitidis* are found in the giant cells. Abscess formation is also seen in the corium. In the nodular or gummatous lesions the histopathology is more like that found in tuberculosis. Little suppuration occurs, and unless the organisms can be demonstrated in the giant cells, difficulty in differentiation may be experienced.

PROGNOSIS

We have no exact figures as to the mortality of primary cutaneous Gilchrist's disease, but the mortality must be quite low, as patients with infection of several years' duration are often seen in whom no ill effects are noted. It is known, however, that the disease may progress to the systemic form through spread by way of the blood stream or lymphatic system.[12] With systemic Gilchrist's disease the prognosis is quite poor. The mortality rate is estimated as being between 80 and 90 per cent. With this in mind, certainly every effort should be directed towards early diagnosis of suspected skin lesions.

THERAPY

Potassium iodide and other forms of iodides have been the drugs of choice in the treatment of this disease for many years, Gilchrist,[11] in 1902, being apparently one of the first to give a report on its efficacy. In studies at Duke Hospital we have found that this drug is, however, not entirely without danger. In patients found to have a marked sensitivity to the organism, spreading of the lesions has been found to occur after administration of iodides. Preliminary desensitization with a vaccine prepared from the *Blastomyces dermatitidis* seems to prevent this. At present all cases are first tested by the use of an intradermal test dose of 0.1 c. c. of a one to one thousand dilution of heat-killed *Blastomyces dermatitidis* vaccine. Then, depending on the degree of reaction present, desensitizing doses of the vaccine are given. An autogenous vaccine is preferable, but not necessary. We have observed as good results with a stock vaccine as have been observed in cases treated by desensitization with autogenous vaccine. After this, iodides are administered by mouth in gradually increasing dosage, but in amount not exceeding five grams of the drug given three times a day.

Local treatment of the lesions is also of value. X-ray irradiation, radium applications, curettage, cauterization, the use of carbon dioxide snow, iodides locally, copper sulphate com-

presses, iontophoresis with copper sulphate, the local use of gentian violet, and various other local forms of treatment have all been tried and have given varying success. In our hands the combined use of desensitization, iodides by mouth, warm compresses, curettage of the margins of the lesions, and x-ray irradiation have seemed to give the best results.

REFERENCES

1. Jacobson, Harry P.: Fungous Diseases, pp. 149-181. Springfield: Charles C. Thomas, 1932.
2. Moore, Morris: Blastomycosis: Report of a Case with a Study of an Etiologic Factor and a Classification of the Organism. Ann. the Mo. Botanical Garden, **20**:79-118, 1933.
3. Gilchrist, T. C.; and Stokes, W. R.: The Presence of an Oidium in the Tissues of a Case of Pseudo-lupus Vulgaris. Bull. Johns Hopk. Hosp., **7**:129-133, 1896.
4. Redaelli, P.; and Cifferri, R.: Gilchristia Dermatitidis (Gilchrist and Stokes) Cif. and Red., the Causative Agent of the American Gilchrist Disease (Dermatitis Verrucosa). Jour. Trop. Med. & Hyg., **37**:280-282 (Sept.) 1934.
5. Conant, Norman F.: Laboratory Study of Blastomyces Dermatitidis Gilchrist and Stokes, 1898. To be published. Personal communication.
6. Gilchrist, T. C.; and Stokes, W. R.: A Case of Pseudo-lupus-vulgaris Caused by a Blastomyces. Jour. Exp. Med., **3**: 53-78, 1898.
7. Martin, D. S.; and Smith, D. T.: Blastomycosis (American Blastomycosis, Gilchrist's Disease): A Review of the Literature. Amer. Rev. Tuberculosis, **39**:275-304 (March) 1939.
8. Conant, N. F.; and Martin, D. S.: The Morphologic and Serologic Relationships of the Various Fungi Causing Dermatitis Verrucosa (Chromoblastomycosis). Amer. Jour. Tropical Med., **17**:533-576 (July) 1937.
9. Moore, Morris: Blastomycosis, Coccidiodal Granuloma and Paracoccidioidal Granuloma: Comparative Study of North American, South American and European Organisms and Clinical Types. Arch. Dermat. & Syph., **38**:163-190 (Aug.) 1938.
10. Martin, D. S.: Complement-Fixation in Blastomycosis. Jour. Infect. Dis., **57**:291-295 (Nov.) 1935.
11. Gilchrist, T. C.: Blastomycetic Dermatitis in the Negro. Brit. Med. Jour., **2**:1321, 1902.
12. Weidman, F. D.; and Ormsby, O. S.: Discussion: American Dermatologic Association Society Transactions. Arch. Dermat. & Syph., **25**:179, 1932.
13. Stober, A. M.: Systemic Blastomycosis: A Report of Its Pathologic, Bacteriologic and Clinical Features. Arch. Int. Med., **13**:509-555, 1914.

DISCUSSION (*Abstract*)

Dr. Everett C. Fox, Dallas, Tex.—Dr. Moseley's paper is very appropriate, since he calls to our attention a condition seen more frequently and distributed more widely than was formerly thought. Attention has been directed to the two forms of Gilchrist's disease and an excellent clinical description given of the lesions of the primary cutaneous type. I feel that all of us should have a little higher degree of suspicion of blastomycosis and should consider this condition more frequently when we see conditions which must be differentiated from tuberculosis verrucosa cutis, bromoderma, superficial malignancy, late syphilitic lesions, and other superficial chronic granuloma.

The usual laboratory procedures used in the diagnosis of blastomycosis demonstrating the blastomyces dermatitidis, either in freshly prepared smears, by culture or by histologic examination of tissues, have been used quite frequently. Drs. Callaway and Moseley add two additional laboratory procedures which may at times be valuable. The complement-fixation test and the diagnostic intracutaneous test are newer procedures. If we keep this condition in mind and make use of these five laboratory procedures, cases of blastomycosis will not escape diagnosis, although at times histologic examination without extremely careful study may not reveal the organisms and the process may pass as either tuberculosis, cutaneous malignancy or other chronic granuloma.

Therapy still consists largely of the administration of large doses of potassium iodide, although x-ray therapy has produced excellent results, especially in combination with the iodides. Carbon dioxide snow, curettage and electrodesiccation have been effective measures. Drs. Callaway and Moseley have suggested that patients be desensitized by giving a vaccine of heat killed blastomyces dermatitidis before starting iodide therapy. This is a new idea which seems very logical.

My experience with blastomycosis has been limited to a small number of cases.

Dr. M. T. Van Studdiford, New Orleans, La.—Unfortunately, we are in about the same spot as Dr. Fox. We do not see new cases. The first ten years that I practiced dermatology we averaged about seven or eight new cases a year at Charity Hospital. For the last five years, we have had one chronic case, a negro boy who has become a morphine addict and who will not let his skin lesions heal. He is our exhibit for class demonstrations.

I do not think iodides in the treatment of blastomycosis are worth 5 cents. They are worse than of no use; they cause exacerbation. If you pick up any text, the first thing it tells you is to administer iodides in large amounts. However, I have seen patients who became worse and worse and worse while taking iodides, and who improved after they were stopped.

The only good effect I have ever obtained in treatment has been with x-rays, x-rays nearly up to the point of cauterizing the tissues. Blastomycosis of the skin goes in cycles: the patient has a rise of infection, it levels off, and no matter what treatment you give him he becomes better, unless you give him iodides. When his condition shows improvement, he thinks he will continue to improve, and usually leaves the hospital for a visit to his home. Then, in a season or two, he returns with an acute exacerbation. I do not know the number of cures we have obtained, but I am speaking of 57 cases which it has been my good fortune to see and treat.

I have cultured blastomyces from the fluid from the pleural cavity and from bursa cavities and put these cultures under the x-ray and poured varying doses of x-rays, from one minute up to an hour, without any effect at all on the growing blastomyces in the cultures.

Diagnostic results from scrapings have been very poor in our hands. If I were to write the chart that Dr. Moseley put up, I would turn it around and I would say take a skin section first. You will find the

blastomyces in the layer of inflammation at the junction with the normal skin. We have scraped some cases as often as twenty times, and even though the best of pathologists examined these scrapings carefully and thoroughly, no blastomyces were found until we had made a skin section.

The systemic cases die, no matter what you do for them. I think it was a Chicago dermatologist who said that one of the worst systemic cases ever seen in Chicago, after receiving a bad prognosis from everybody, went out West to New Mexico, lived in the open, took no treatment, and returned after five or six years a well person.

One of the very interesting points brought out in this paper is that in cases of lupus vulgaris the blastomycetes are secondary invaders. We have found this condition in two cases of lupus vulgaris, one in an elbow lesion, the other in the fold adjacent to the ear.

The results reported in this paper seem to show that vaccine therapy is very helpful.

Dr. Harry M. Robinson, Baltimore, Md.—I am particularly concerned with what Dr. Van Studdiford said concerning potassium iodide medication. In my hands it has been uniformly successful. I have but lately had an office patient who scratched herself on a nail and developed blastomycetic dermatitis. This patient cleared up entirely under potassium iodide.

To some of the patients I have given x-ray therapy, but most of them have not received this form of therapy. The one patient, for instance, whose case was published in the *Archives of Dermatology and Syphilology* in 1933 as one of "Blastomycetic Dermatitis by Lymphatic Extension," involuted entirely under small doses of potassium iodide, ten grains three times a day, and although this patient had one recurrence due to lapse in treatment, he has since returned, resumed treatment and there is now no evidence of the disease. I would therefore suggest that potassium iodide be given a trial in each case, as well as x-ray.

Dr. Moseley (closing).—I quite agree with Dr. Van Studdiford about the dangers of potassium iodide therapy. We similarly have observed that many of the patients who were treated with iodides began to run fever, lose weight, and the lesion spread during the period of iodide administration. The patient was then skin tested to an autogenous heat-killed vaccine of blastomyces dermatitidis. He was found to react in a markedly sensitive manner. It was therefore thought that with resolution of the granulomatous lesion under iodide administration that he was absorbing sensitizing products from the fungi. Desensitization with the vaccine was started, and as you can see his fever began to subside, he began to gain in weight, the lesion became arrested and subsequently healing occurred. He later received a subsequent course of iodide with no spread of his skin lesion or other untoward reactions and went on to complete cure.

This is the point I wanted to stress during the reading of our paper, that if iodides are to be used, the patient should first be skin tested to either an autogenous or stock vaccine of the *Blastomyces dermatitidis*. Then, depending on the degree of sensitivity exhibited, desensitization should be instituted. After desensitization has been accomplished iodides may be safely given, and with good therapeutic results.

STUDIES IN OBSTETRIC ANALGESIA*

By DONALD M. PATON, M.D.
Houston, Texas

The labors from which this material was obtained comprise two separate series conducted in separate institutions. The first series of 555 cases was taken from the University of Texas hospital service at Galveston in 1935-36. The second series of 403 cases was obtained from the Jefferson Davis Hospital in Houston during the summer of 1938. In the first series there is a group of 153 private patients in whom labor was managed by a number of different men. There was no uniformity of procedure in the majority of these private cases in regard to either delivery or medication and therefore they are excluded from the discussion. A number of these private patients were included because their management was very similar to that of the ward patients.

All ward primiparas and those in the small group of private patients mentioned above were delivered by routine elective low forceps and episiotomy. This procedure in our opinion is an important step in obtaining successful analgesia and amnesia, for while spontaneous delivery would occur, it is certain that amnesia could not be maintained throughout delivery without the help of an anesthetic. However, in the case of some multiparas the analgesia and amnesia were complete without an anesthetic's having been used. There is no implication here that analgesic medication in any way interfered with normal delivery or increased the percentage of operative deliveries in our series, the number of operative deliveries in our series being no greater than normal. It is our belief that operative interference is less frequent in cases where amnesia is obtained because the temptation for untimely and ill-advised meddling does not exist.

Ether was the standard anesthetic for both delivery and repair. Chloroform was occasionally used. Gas was given as an induction anesthetic for sections. Anesthesia could not be used for patients with precipitate delivery and was often not required for multiparas under deep

*Read in Section on Anesthesia, Southern Medical Association, Thirty-Second Annual Meeting, Oklahoma City, Oklahoma, November 15-18, 1938.

*The author wishes to express appreciation to the Riedel-de-Haen Company for supplying sodium amyl beta bromallyl barbiturate, "sigmodal," used in this work.

analgesia. Local anesthesia was employed in delivering the majority of eclamptics.

First-stage analgesia with amnesia was the chief aim in the management of all cases unless a contraindication existed. Approximately 75 per cent of the first series and 50 per cent of the second series received analgesic medication. The groups that did not receive medication included all patients who arrived at the hospital far advanced in labor, patients with extremely rapid labor, eclamptics with convulsions, and patients who were sectioned. In the first series, patients in premature labor did not receive much medication, though this was not true of the second series which contained a large percentage of premature labors. There are several reasons for the difference in the percentage of patients receiving analgesia in the two series. The Jefferson Davis Hospital draws patients from a more metropolitan area and a number of patients are seen for the first time when admitted to the ward, often in advanced labor. Furthermore, as many as possible of the normal multiparas are delivered at home by the medical students. Many multiparas, knowing this fact, arrived at the hospital when labor was so far advanced that they could not safely be sent home and incidentally, when they were beyond the stage of receiving analgesia with safety. Twenty-nine per cent of the patients at the Jefferson Davis Hospital were delivered within two hours after admission. In the interest of reducing infection no analgesia was used unless the patient had had an enema. This was also a factor in reducing the number of patients who received medication.

Table 1

		Per Cent
Total primiparas	410	43
Total multiparas	548	57
	958	

Forceps	Primipara	Per Cent	Multipara	Per Cent	Total
Low	262	64	43	8	305
Mid	18	4	6	1	24
Episiotomy	332	81	52	9	384

	Primipara and Multipara	Per Ct.
Twins	18	2—
Sections	20	2+
Breech	35	4—
Version	5	0.5
Face	3	0.3
Mortality	6	0.6

Out of the total of 958 deliveries, 610 patients received some type of analgesia. In our previous report (the first series) rectal ether, morphine-hyoscine, pentobarbital ("nembutal")-hyoscine, and hyoscine-sodium iso-amylethyl barbiturate ("amytal") were the principal combinations employed. No accurate record was made of restlessness in these patients. It can safely be estimated that nearly 50 per cent were restless during labor. This aspect of obstetric analgesia constitutes an important factor in the management of the private patient, especially where the family cannot be excluded from the labor room. It was therefore decided that in the second series some effort should be made to find a combination of drugs which would provide adequate amnesia, and minimal disturbance, with safety to the baby.

With this in mind we included "pantopon" in the pentobarbital-hyoscine combination and also used sodium amyl beta bromallyl barbiturate ("sigmodal") in another group. Having closely observed and followed a number of private patients treated with "pantopon" grains 1/3 and pentobarbital grains 6, we realized that while such medication could give good amnesia in a private institution where each patient in labor has a special nurse, similar results were not to be expected in a charity hospital. At the suggestion of Dr. E. D. Embree, of Houston, who has had an extensive experience in obstetric anal-

Table 2

TYPES OF ANALGESIA

	Primipara	Per Ct.	Multipara	Per Ct.	Total	Per Ct.
Rectal ether	73	18	73	13	146	15.3
Morphine-hyoscine	53	13	15	3	68	7.0
Hyoscine-sodium iso-amylethyl barbiturate ("amytal")	23	6	15	3	38	4.0
Pentobarbital-hyoscine	62	15	69	12.6	131	13.5
Pentobarbital-hyoscine-"pantopon"	45	11	19	3.4	64	6.7
"Sigmodal"	32	8	13	2.7	45	4.5
Pentobarbital	9	2	3	0.5	12	1.3
Sodium "amytal" Sodium "amytal"-morphine Morphine Pentobarbital-"pantopon" Pentobarbital-hyoscine-morphine Hyoscine-"pantopon" Pentobarbital-morphine	33	8	76	13.3	109	11.4
	328	91	284	51.4	610	64

gesia and anesthesia, we used an initial dose of "pantopon" grains 1/6, hyoscine grains 1/200, and pentobarbital grains 6. Thus the doses of pentobarbital and hyoscine were slightly lower than when these drugs were used without "pantopon." The average initial dose was as given above, although occasionally a slightly smaller amount was used. Additional pentobarbital was given in many instances, bringing the average amount of pentobarbital to grains 7.5 for primiparas and grains 7.2 for multiparas. This combination of drugs was used in 64 cases.

"Sigmodal" was employed in 45 cases. The technic and the routine of administration were those advised by Dr. Emmert, of St. Louis. The average dose for primiparas was 10 c. c. and for multiparas, 10.7 c. c. The increase in the amount given to the multiparas was due to the fact that several patients had to have a small additional dose because of a long labor.

Pentobarbital with hyoscine was used in 131 cases in all, 83 in the first series and 48 in the second. The initial dose was pentobarbital grains 7½, hyoscine grains 1/150. Additional pentobarbital was given when necessary. The average dose was grains 9.3 and grains 7 for primiparas in the first and second series, respectively. Likewise for multiparas the average was grains 8 and grains 7.4. The use of smaller dosages in the second series is attributed to the fact that "pantopon" was being given as often as possible. When a patient was advancing rapidly, "pantopon" was usually omitted so that cases with short labors requiring less medication often fell into the pentobarbital-hyoscine group. The initial dose given in such cases was generally sufficient without additional medication.

Rectal ether was the most frequently used analgesic in the first series, being given to 130 patients, usually in late first-stage labor. Its apparent importance here is due to the fact that it was used as a substitute for other types of analgesia which might have been dangerous for the baby if given so late in labor. The average dose was ether ounces 2½ and olive oil ounces 1½. It was sometimes combined with sodium iso-amylethyl barbiturate ("amytal"), morphine, etc. Usually these other drugs had been used so long before delivery that their effect upon the baby could be considered negligible. Rectal ether in the second series was quite limited (16 cases). Twelve patients who would have received rectal ether according to its use in the first series were given pentobarbital grains 6. Many other patients received no medication because of the rule that every patient was to have an enema if possible before delivery.

The earliest point in labor at which it was possible to start the analgesic medication without stopping labor was fairly constant for all the drugs used. It is to be remembered that rectal ether was employed often as a late first-stage or even second-stage analgesic. Pentobarbital with hyoscine (in the second series) was started later in the course of labor than the other drugs because, as stated before, it was given to those patients who were advancing too rapidly for the safe use of "pantopon" in the combination. The

Table 3

DETAILS OF ANALGESIC ADMINISTRATION

	Primipara				Multipara			
	Dilatation (fingers)	Time hr.	min.	Dose	Dilatation (fingers)	Time hr.	min.	Dose
Rectal ether (first series)	4.5	2	15	2½ oz.	5	1	20	2½ oz.
Rectal ether (second series)	4.5	1	30	2½ oz.	5	1		2½ oz.
Morphine-hyoscine	2.5	5	40	inj. 2	2	3	20	inj. 1.5
Hyoscine-sodium iso-amylethyl barbiturate	2.5	5	10	inj. 1.5	2.5	3		inj. 1.5
Pentobarbital-hyoscine (first series)	2	4	10	9.3 gr.	2	3	50	8 gr.
Pentobarbital-hyoscine (second series)	3+	3	45	7 gr.	3—	4	15	7.4 gr.
"Pantopon"-pentobarbital-hyoscine	2.5	5		7.5 gr.	2.5	3	15	7.2 gr.
Pentobarbital	3—	2		5.6 gr.	2		45	6 gr.
Sodium amyl beta bromallyl barbiturate	2.5+	6		10 c. c.	2+	4		10.7 c. c.

same statement applies to pentobarbital given without complementary drugs. Pentobarbital with hyoscine in the first series was started a little earlier than other analgesics.

Morphine with hyoscine, commonly known as twilight sleep, was used in 68 cases. This was given by one of two methods. The first of these is identical with the routine followed at St. Louis Maternity Hospital. It was given thus: sodium iso-amylethyl barbiturate up to grains 12 if necessary as a preliminary. Initial dose:

Primipara (3½ fingers dilated) morphine grains 1/6 or 1/8, and multipara (2½ fingers dilated) hyoscine grains 1/150.

Then hyoscine grains 1/150 at 45 minute intervals for 2 doses, the second being reduced to grains 1/300 if sufficient. After this, hyoscine grains 1/300 every 1½ hours according to narcosis.

Morphine was never repeated. When twilight sleep was begun before the specified dilatation, labor often stopped; if much after this stage, poor amnesia and a narcotized baby were often the result. If labor was too far advanced for the safe use of twilight, rectal ether was substituted or sodium iso-amylethyl barbiturate was continued with hyoscine injections. The latter cases will be discussed below.

The second method of giving morphine and hyoscine was to start with the same initial hypodermic dose as above plus sodium iso-amylethyl barbiturate grains 6 by mouth, timed according to the degree of pain. At this stage the cervix was usually at least one finger dilated. Subsequent doses usually at one to two hour intervals consisted of sodium iso-amylethyl barbiturate grains 3 alone or with hyoscine grains 1/150 or 1/300, or hyoscine alone.

The only noticeable differences between the two methods were: (1) A few more babies required resuscitation where the first method was used. (2) Amnesia began later with the first method because sodium iso-amylethyl barbiturate as a preliminary to twilight sleep was frequently inadequate even for relief of pain.

Thirty-eight patients, mostly private, received hyoscine with sodium iso-amylethyl barbiturate, morphine being purposely omitted. These drugs were administered by the two methods described above for twilight. The second method was more applicable to this form of analgesia, especially in multiparas. Ward cases were usually managed with cervical dilatation as an index for beginning medication, private cases by degree of pain.

The time which elapsed between the administration of the medication and the delivery showed no significant variation. In general it depended upon the stage of labor at which the analgesic, considered most suitable for that patient, was begun. This is exactly what would be expected. It is probable, but not at all conclusive, that the addition of "pantopon" to the pentobarbital-hyoscine combination caused the labor to be slightly slower than when pentobarbital-hyoscine alone was used.

Amnesia was considered satisfactory if the patient recalled nothing at all of the labor, or only a few isolated events. The degree of amnesia varied little as far as the pentobarbital groups were concerned. It was complete in a few more cases where "pantopon" was included. The pentobarbital groups and sodium amyl beta bromallyl barbiturate were more applicable to multiparas than the other drug combinations. Hyoscine with sodium iso-amylethyl barbiturate was fairly satisfactory. The low figure of satisfactory amnesia obtained in only 65 per cent of the patients who received morphine-hyoscine is not a true representation of the efficiency of this analgesic. Our previous experience with twilight sleep enables us to make this statement with every confidence. We believe the figure should be 80 to 85 per cent. Pentobarbital without complementary medication was used in so few cases that no fair comparison of results can be drawn. Rectal ether was used as a late first-stage or occasionally a second-stage analgesic and so will not be discussed. Sodium amyl beta bromallyl barbiturate produced a satisfactory amnesia in 65 per cent of primiparas, 60

Table 4

DEGREE OF AMNESIA

	Primipara Per Cent	Multipara Per Cent	Average Per Cent
Rectal ether (first series)	46.6	38.8	45.4
Rectal ether (second series)	44.4	33.3	41.7
Morphine-hyoscine	68.4	57.1	65.3
Hyoscine-sodium iso amylethyl barbiturate	83.3	66.6	77.7
Hyoscine-pentobarbital (first series)	92.0	74.3	80.8
Hyoscine-pentobarbital (second series)	83.3	81.3	82.6
Pentobarbital-hyoscine-"pantopon"	85.4	85.7	85.5
Pentobarbital	62.5	50.0	60.0
Sodium amyl beta bromallyl barbiturate	65.2	60.0	63.6

per cent of multiparas, with an average of 63.6 per cent. We are sorry that we cannot report a better result than that. Perhaps this barbiturate requires more careful attention than other analgesics.

Before calculating the percentage of satisfactory results obtained from any analgesic in the series (except twilight sleep) we discarded all cases where there was an obvious error in technic of administration, selection of the case, or in determining the progress of labor. Furthermore, cases were discarded if the patients had not been properly prepared. This was highly important in using "sigmodal." Other cases were thrown out because the medication produced excellent amnesia at the beginning only to fail because of the negligence of the attendant to repeat the dose. A few cases were included in calculating the final results where there was some doubt about the technic. It is probable that much better results could be obtained in a private institution with an experienced special nurse in constant attendance upon each patient. It must be realized in reviewing all these results that the circumstances were not ideal. Therefore, while excellent amnesia obtained under these conditions speaks well for a drug, it does not necessarily follow that a poor amnesia condemns it. We wish to stress the importance of using these drugs only in a well-regulated hospital with an experienced personnel.

In reviewing the degree of restlessness in the patients, we found a marked difference in the analgesics employed. In the sodium amyl beta bromallyl barbiturate group restlessness was either absent or only slight in 63 per cent. This figure fell to 41 per cent with pentobarbital-hyoscine-"pantopon." With pentobarbital-hyoscine it fell to 31 per cent. Twenty per cent of the "sigmodal" group were extremely restless; 29 per cent of the pentobarbital-hyoscine-"pantopon" group; and 39 per cent of the pentobarbital-hyoscine group. We think these differences are enough to be significant.

Table 5

DEGREE OF RESTLESSNESS

	None or Slight Per Cent	Average Per Cent	Extreme Per Cent
Pentobarbital-hyoscine-"pantopon"	41.1	29.4	29.4
Pentobarbital-hyoscine	30.5	30.6	38.9
Sodium amyl beta bromallyl barbiturate	62.8	17.1	20.0

Likewise the number of resuscitations in the babies of the various groups shows remarkable contrast. All babies were classed as resuscitated whenever external stimulation or use of a bulb syringe in the mouth failed to produce cry and respiration. It was customary to use a tracheal catheter if spontaneous breathing did not occur. The amount of medication and the length of first-stage labor did not seem to increase the number of resuscitations unless there was a difficult forceps delivery or other complication. Only one baby (2.2 per cent) in the "sigmodal" group had to be resuscitated. Pentobarbital-hyoscine babies had 7.3 and 6.4 resuscitations in the two series, respectively. It is interesting to note that the two highest figures occurred in the two groups employing an opiate, namely: pentobarbital-hyoscine-"pantopon," 22 per cent, and morphine-hyoscine, 24 per cent. In the sodium amyl beta bromallyl barbiturate group the sleepy baby weighed less than six pounds. In the pentobarbital-hyoscine-"pantopon" group two of the resuscitated babies were prematures, six weighed six pounds or less, and two of the babies which weighed more than this were subjected to difficult deliveries. In other cases where the medication was apparently heavily concentrated into a short period before delivery or where the usual dose was given only very shortly before delivery, sleepy babies were obtained. We know from our experience in private practice that the routine use of gas anesthesia administered by a trained obstetrical anesthetist could reduce these figures by at least a half.

As for any detrimental effect of analgesia on the mothers, suffice it to say that the medication was in no case accountable for morbidity or death. In the first series one patient died from

Table 6

RESUSCITATION OF BABIES

	Per Cent
First series	
Rectal ether	5.2
Morphine-hyoscine	23.5
Hyoscine-sodium iso-amylethyl barbiturate	13.1
Pentobarbital-hyoscine	7.3
Second series	
Pentobarbital-hyoscine-"pantopon"	21.9
Pentobarbital-hyoscine	6.4
Sodium amyl beta bromallyl barbiturate	2.2
Pentobarbital	0
Rectal ether	0

shock after a premature separation of the placenta. This woman was evidently extremely toxic. During labor she had received 6 grains of sodium iso-amylethyl barbiturate. In the second series only one death occurred among the patients who received analgesia. This woman had sodium amyl beta bromallyl barbiturate during early labor and 12 hours later was given pentobarbital and hyoscine. The delivery was complicated by retention of the placenta and the patient died two weeks later from septicemia.

Concerning the fetal mortality little comment is needed. In the first series only two deaths occurred in cases where analgesics could even be suspected. One of these babies was delivered from a colored primipara who had had eclamptic convulsions. The baby was delivered several days after the control of the convulsions. Labor and delivery were uncomplicated, the patient having received an average morphine-hyoscine narcosis. The baby failed to breathe. The heart beat for one-half hour after birth. All methods of resuscitation were tried. The other death occurred in a full-term baby delivered by low forceps and episiotomy from a colored primipara in labor for 17 hours under average effective morphine-hyoscine narcosis. The baby gasped a few times and died. Autopsy findings were negative.

In the second series there were 13 fetal deaths among babies delivered by patients who had had analgesia. In every instance there was sufficient cause for death even if no drugs had been used. There were 3 deaths in the pentobarbital-hyoscine-"pantopon" group, 3 in the pentobarbital-hyoscine group, 5 where pentobarbital was used alone, and 2 in the sodium amyl beta bromallyl barbiturate group. Factors contributing to these deaths are presented in the accompanying chart.

Table 7

FETAL DEATHS

	Pentobarbital-hyoscine-"pantopon"	Pentobarbital-hyoscine	Pentobarbital	Sodium amyl beta bromallyl barbiturate ("sigmodal")
Premature				
Stillborn		1	1	1
Died			1	
Premature and lues				
Stillborn			1	
Lues				
Stillborn	1			
O.B. Accident				
Stillborn	1	2	1	
Died			1	
O.B. Accident, Premature, Toxemia				
Died	1			
Congenital Defect				
Died				1
	3	3	5	2

CONCLUSIONS

(1) Pentobarbital - hyoscine - "pantopon" and pentobarbital-hyoscine gave satisfactory amnesia in 80 to 85 per cent of cases. Hyoscine-sodium iso-amylethyl barbiturate was effective in 77 per cent, morphine-hyoscine in 65 per cent, and sodium amyl beta bromallyl barbiturate in 64 per cent.

(2) There was no increase in the incidence of operative delivery.

(3) Sodium amyl beta bromallyl barbiturate was safer for the baby than the other analgesics used. Pentobarbital with hyoscine was safer than morphine-hyoscine, pentobarbital-hyoscine-"pantopon," or sodium iso-amylethyl barbiturate-hyoscine. Danger to the baby is negligible in the hands of one trained in the use of these analgesics.

(4) Twilight sleep used in a toxic patient may provide a definite threat to the life of the baby.

(5) Sodium amyl beta bromallyl barbiturate, sodium iso-amylethyl barbiturate-hyoscine and combinations of drugs employing pentobarbital could be started a little sooner in labor than twilight sleep and were therefore preferable to it in multiparas.

(6) "Sigmodal" caused the least restlessness in labor. The use of "pantopon" with the pentobarbital-hyoscine analgesia diminished appreciably the amount of restlessness in that group.

I wish to express my appreciation to Dr. Willard Cooke for permission to use cases which I managed while I was obstetrical resident at John Sealy Hospital; to Dr. F. J. Iiams for allowing me to run my second series of cases during his period as chief of service at the Jefferson Davis Hospital; and lastly, to the interns, medical students and nurses, without whose willing cooperation this work would not have been possible.

DISCUSSION (*Abstract*)

Dr. M. J. Serwer, Oklahoma City, Okla.—We have as yet no analgesic or amnesic that is satisfactory in all cases. Thus, as Dr. Paton has shown, each patient

should be evaluated individually and given sedatives accordingly; realizing that there is a price she must pay, calculated in terms of added risk to mother and baby, for the relief afforded.

I personally make no attempt to give my patient a painless labor. She and her relatives are told an attempt will be made to ease her pains so that the memories of labor will not be a nightmare; that sedatives will be given up to the point of danger, and that this point may not always coincide with her desires. In this way I am relieved of much meddlesome interference on the part of relatives.

I am opposed to the use of large doses of barbiturates because of the cyanosis I have occasionally encountered. I have also noticed a marked increase in the number of cervical tears following the use of these drugs.

I have used several of the methods Dr. Paton has mentioned, but somehow I always revert to morphine and scopolamine. Perhaps I know more about them and can use them with greater efficiency. The marked narcosis attributed to opiates is usually due, I believe, to the added insult of operative interference.

In regard to the use of morphine in eclampsia, I am not concerned so much with the baby as I am with the mother, since the fetal mortality is unusually high from toxemia alone and my use of the drug depends entirely upon the mother's needs.

I have not used rectal ether in many years, as I feel that the difficulty in its proper administration, retention and resulting proctitis far outweigh its advantages.

As Dr. Paton has said, it is important that the patient never be given a sedative without first being given an enema.

Dr. Mary Catherine Baldwin,, Riverside, Calif.—It is most necessary for the patient and her obstetrician to understand each other. Patients, for the most part, are anxious first of all to have a robust child, and secondly to come through without impairment themselves. Usually, if properly instructed, the mother is more than willing to play her part if she thoroughly understands that every help that is safe for her and the baby will be given. There is never in life any situation which is not better met in a valiant and enlightened state of mind. It has been my constant observation that women who are prepared mentally for labor and delivery are more than half way to their goal, other things being equal.

Expectant mothers are much like very young girls; they are consumed with a desire to know more of their approaching delivery but, like young girls, are often very shy about asking questions. It seems to me that we are highly rewarded for the time we spend educating these expectant mothers, as entirely too much false education takes place over tea and bridge tables.

Did you ever contemplate the two words, "labor" and "delivery?" It did not happen by chance that the two main processes of this miracle called "birth" were so named. Spiritually, I believe we all would choose to feel that we were playing a somewhat active part in the process. This may seem a somewhat too idealistic attitude to take of the situation, but it is the idealist who brings about the worth-while changes in this world.

The use of pentobarbital sodium in the first stage of labor combined with ether-oil or with ether-oil and paraldehyde is certainly a safe method for both mother and child. If this is then combined with an inhalation anesthesia of nitrous oxide and oxygen or cyclopropane and oxygen for the second stage, it seems to me that we have an almost perfect combination.

There is another factor which is of paramount importance and is all too infrequently recalled. It is, of course, impossible for a busy obstetrician to remain with each patient for the complete course of her labor, but he may have a personal representative with her. There probably are multiple examples of this fine team work elsewhere, but I know of one very outstanding obstetrician who employs a thoroughly trained obstetrical nurse who knows each patient: all her idiosyncrasies, strengths and weaknesses. When a patient goes into labor Miss T. goes immediately to the hospital, where she personally conducts all preparation of the patient and because she is loyal to her employer and well trained, she keeps the patient in the best possible state, and when she calls the obstetrician, he knows he is needed. For years this combination has produced fine work: operative deliveries cut to a minimum, almost no fetal or maternal morbidity. The obstetrician feels that his attendant more than pays her own salary (which, by the way, is a very ample one) in the confidence it gives him and his patients. This attendant is extra help at the office during days when she is not catching up on lost sleep. It has been effectively shown that a good attendant helps a parturient by giving that confidence which is needed in the sometimes long stretches of slow first stages even in the presence of effective analgesia.

Here we again come to the same conclusions that many writers in the now voluminous literature on the subject do:

(1) Proper analgesia and good obstetrics will convert a primipara into a competent multipara.

(2) There is not yet the perfect analgesic. Many combinations of drugs are used which the proponents call synergism and the critics call polypharmacy.

(3) It is only fair to say that morphine best relieves the pain.

(4) Scopolamine produces amnesia even if not sleep, but it often also produces restlessness.

(5) Ethylene, nitrous oxide, ether, vinyl ether and cyclopropane will produce partial or complete anesthesia.

(6) Paraldehyde is the safest hypnotic.

(7) Too frequently analgesia is discarded not because of its dangers, but because of its exacting demands upon the obstetrician, and this latter objection may be largely removed by the special attendant described.

Dr. Paton (closing).—I agree with Dr. Baldwin that there is no perfect obstetrical analgesic and, like Dr. Serwer, I do not promise any patient a painless labor, for I think any attempt to produce that is attended by certain risks. I believe that barbiturates are helpful in treating eclampsia, likewise morphine is a powerful aid. I may not have made myself clear in giving my opinion of twilight sleep in such cases. I do not like to use morphine and hyoscine as an analgesic for labor in toxic cases where the toxemia is under control and the baby is in apparently good condition. I believe that barbiturates do not provide as much added insult here as the opiates. However, for the control of the actual convulsions where our concern is naturally more for the mother than for the baby, I always use morphine.

SERODIAGNOSTIC TESTS FOR SYPHILIS AS PERFORMED IN STATE LABORATORIES IN 1938 AND 1939*

A REPORT OF THE COMMITTEE ON EVALUATION OF SERODIAGNOSTIC TESTS FOR SYPHILIS

By H. H. HAZEN, M.D.
Washington, D. C.
THOMAS PARRAN, M.D.**
Washington, D. C.
J. F. MAHONEY, M.D.†
Washington, D. C.
ARTHUR H. SANFORD, M.D.
Rochester, Minnesota
F. E. SENEAR, M.D.
Chicago, Illinois
WALTER M. SIMPSON, M.D.
Dayton, Ohio
and
R. A. VONDERLEHR, M.D.‡
Washington, D. C.

At a time considerably antedating the general increase of interest in the campaign against syphilis, it was entirely apparent that ultimate control would be dependent, in large measure, upon the accuracy with which serodiagnostic work was carried out in the laboratories of the country. It was apparent, too, that there existed a wide variation in the standard of service being given by laboratories serving large population groups. The need for accurate information regarding the relative efficiency of serologic tests from which corrective measures might be deduced if necessary led to the formation of the Committee on Evaluation of Serodiagnostic Tests for Syphilis. This was accomplished by a cooperative arrangement between the U. S. Public Health Service and the American Society of Clinical Pathologists. This Committee has continued to function up to the present time.

The initial study of the Committee[1] was undertaken to evaluate the several distinctive technical methods developed by American serologists. Test material for this survey included both spinal fluids and whole blood specimens which were obtained from known syphilitic and normal, presumably nonsyphilitic donors. Specimens taken from individuals affected by metabolic disturbances or pathological conditions which might adversely influence syphilis serologic tests formed a significant part of the nonsyphilitic donor group. As a result of the original study, five of the methods were selected to serve as controls in future studies because of their relatively high ratings, their practical adaptability, the availability of complete descriptive literature, and their widespread use. These were the methods of Eagle, Hinton, Kahn, Kline, and Kolmer.

With this foundation, the subsequent work of the Committee[2 3] was designed to survey the standards of efficiency maintained in laboratories doing a large volume of serologic work. Participation in the surveys was limited to organizations serving the profession in large population groups. An equally important objective was obtained by extending an opportunity to participate in serodiagnostic evaluation studies which afford the laboratories a basis for comparing their results with those produced by the originators of the respective control technics. The basic intent of the work has been informative rather than critical.

In the early work of the Committee, index figures based upon percentage calculations of positive findings in known syphilis and negative findings in presumably normal donors were utilized as a means of expressing sensitivity and specificity. As an entirely equitable method of evaluating doubtful results was not available, all such findings were considered as negative in arriving at the specificity and sensitivity ratings.

Subsequently a second type of analysis was added. This consists of a determination of complete agreement, partial agreement and complete disagreement between the results of the participating laboratory and the appropriate control. In this analysis only the specimens which were tested in both laboratories are considered.

PROGRESS OF WORK

The results of the early surveys conducted by the Committee seemed to permit some rather definite inferences. Judging from the survey specimens alone, it appeared evident that the variations in results obtainable in different laboratories testing identical specimens were probably more pronounced than anticipated. When to the picture was added a detailed description of the technical method employed, some logical

---

*Read in Section on Dermatology and Syphilology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

**Surgeon General, U. S. Public Health Service, Chairman.

†Senior Surgeon, U. S. Public Health Service.

‡Assistant Surgeon General, U. S. Public Health Service.

reasons for the confusion were apparent. In some instances of poor or indifferent performance, reliance was being placed upon obsolete or outmoded technics. Some of these, especially complement-fixation procedures, were entirely incapable of modernization. Some fairly adequate methods were being operated at levels of efficiency considerably below those which the methods were basically capable of attaining. In other cases a decrease in the standard of performance seemed to spring from the introduction into the technic of personal modifications and short cuts which had been developed and utilized almost entirely for the convenience of the operator. Few, if any, of this latter type of technical modification gave evidence of having been adequately studied as to their effect upon other phases of test procedure or as to their ultimate effect upon test results. In some cases there was adherence to test methods which had long been abandoned by the originators. On the other hand, in the tabulation of results produced in some laboratories which were under the guidance of well-trained and skillful serologists or in which the technic employed conformed in a reasonable degree to the technical precepts advocated by the originator, a higher degree of consistency was apparent. Many of the discrepancies in this latter group could be attributed to a difference in interpretation of findings and possibly to a justifiable degree of conservation in utilizing the doubtful range, both of which phases are readily capable of a satisfactory adjustment.

As a direct result of these early findings the Committee was able to formulate a program which seems to be well adapted to the needs of the situation. The major tenets of the plan are:

(1) The abandonment of obsolete and outmoded technical methods.

(2) The rigid adherence to the details of technic as prescribed by the originators of standard or widely used serodiagnostic methods. (Full description of the technic of each test will be found in Supplement No. 11 of Venereal Disease Information, available from the U. S. Public Health Service or the Government Printing Office, Washington, D. C.)

(3) The discouragement of the use of personal modifications and presumably time-saving short cuts.

(4) The provision of an opportunity for state laboratories to determine annually the efficiency of their respective serologic test performances, with the underlying hope that each state would, in turn, offer a similar opportunity to municipal, hospital and private laboratories.

(5) The making available of training facilities in serology for technical personnel.

It is not intended that research in the field of serology be interdicted, although much of this type of effort may well be left to those fortunately situated organizations which have access to the laboratory and clinical facilities essential to this type of work.

The studies of 1938 and of 1939 have not been previously reported. The method used for the selection of donors, the collection and distribution of blood samples, and the analysis of reports in these studies closely followed the procedures outlined in previous Committee publications.

CONTROL LABORATORIES

In both sets of studies there served as controls: Dr. Harry Eagle, who performed the Eagle complement-fixation and the Eagle flocculation tests; Dr. William A. Hinton, who performed the Hinton flocculation test; Dr. Reuben L. Kahn, who performed the Kahn standard and the Kahn presumptive tests; Dr. Benjamin S. Kline, who performed the Kline diagnostic and the Kline exclusion tests; and Dr. John A. Kolmer, who performed the Kolmer complement-fixation test.

PARTICIPATING LABORATORIES

In the 1938 study, 96 test procedures were included for evaluation. These originated from 46 laboratories, representing 44 states and the District of Columbia. There were 33 complement-fixation methods, 49 diagnostic flocculation tests, 10 supersensitive (exclusion or presumptive) flocculation tests and 4 additional flocculation tests that could not be accurately classified, since they followed no known standard technic.

In the 1939 study, 38 state and 3 public health service laboratories participated. A total of 97 test procedures were carried out, 31 of which were complement-fixation and 66 flocculation procedures. The number of laboratories adhering to standard technics has increased greatly since 1938. Only 12 of the 43 which failed to follow the authors' rules in 1938 remain in this undesirable category.

The majority of the state laboratories performing the flocculation tests in the 1939 study adhered very closely to the latest technics recommended by the originators. However, 2 state laboratories did report flocculation tests which adhered to no established technic. The importance of adhering to the technic described by the originator of the test has been discussed elsewhere in this paper.

SENSITIVITY OF CONTROL PERFORMANCES

The level of sensitivity of the control performances in 1939 as compared to 1938 was somewhat higher. Evidently the 1939 group of donors contained a greater number of individuals with more reagin in their blood. The relative position of the control performances as regards sensitivity was somewhat altered in 1939. The Hinton test, which for a number of years had been the most sensitive, this year took a position below the Kline exclusion test and the Kahn presumptive test. The positions of the Eagle complement-fixation test and of the Kahn standard test were reversed by their respective findings in the 1939 study. The following list displays the relative sensitivity of the controls in 1938 and 1939:

	1938	1939
Kline exclusion	83.3	91.0
Kahn presumptive	79.9	87.6
Hinton	83.9	85.5
Kolmer complement-fixation	78.2	83.4
Eagle microflocculation	77.5	82.4
Eagle macroflocculation	.....	80 2
Kline diagnostic	73.4	78.7
Kahn standard	70.5	77.4
Eagle complement-fixation	72.2	73.9

SPECIFICITY OF CONTROL PERFORMANCES

In the 1938 study, none of the control serologists reported a single instance of a false positive or a false doubtful reaction.

In the 1939 evaluation study, all of the control serologists, except two, had a perfect record in this respect. The Kline exclusion test was penalized by the appearance of a donor whose blood gave some degree of positivity to all Kline tests. The Kline diagnostic procedure was doubtful. A repeat specimen gave almost identical results. This case appears to present a biologic false positive reaction confined exclusively to the Kline technic in all hands, inasmuch as all other procedures gave negative results.

One false positive report emanated from Hinton's laboratory. As all other control tests and the Hinton tests done in other laboratories were universally negative, it would seem probable that this represents a laboratory error rather than a biologic false positive reaction.

It is worthy of note that in four years there have been but four false positive reports submitted by the control serologists. This simple fact shows what laboratories can and should do. If a laboratory turns in false positive reports, that laboratory and not the method should be indicted.

CRITERIA FOR SATISFACTORY PERFORMANCE

The Committee set the criteria for satisfactory results as follows:

For sensitivity (the percentage of true positive reactions from known syphilitic donors), the result must not be more than ten points below that of the control laboratory. For example, if the control laboratory had a sensitivity of 91.2 per cent, the lowest rating that could be considered as satisfactory would be 81.2 per cent.

For specificity (the percentage of negative and doubtful reactions from presumably nonsyphilitic donors), the result must not be lower than 99 per cent.

It is very encouraging to observe that whereas in 1938, 30 state laboratories were unsatisfactory in their performance of at least one test, only 22 were unsatisfactory in 1939. Eighteen of these 22 laboratories have expressed dissatisfaction with their results and have taken steps to improve them.

DOUBTFUL REPORTS

Because of the fact that no agreement existed among the various serologists as to what penalties or awards should be given for doubtful reactions, the Committee has given a negative rating to all such reports. It is fully realized that false doubtful reports on normal sera should count definitely against a laboratory. It is also realized that in known cases of syphilis a doubtful reaction may be of great value. Senear[4] has admirably discussed this problem in a recent paper.

WORK IN STATE LABORATORIES

The first serodiagnostic evaluation study in which most of the state laboratories participated (1937) demonstrated conclusively that far too many laboratories of the country were operating at a questionably satisfactory or wholly unsatisfactory level of efficiency.

In 1938, the results from 10 state laboratories approximated the results of the control laboratories; 5 additional state laboratories re-

ported results which were deemed satisfactory; and 30 gave results which were unsatisfactory.

In 1939, the 10 laboratories approximating the results of the control laboratories in 1938 did not participate in the study. During the 1939 study, 3 state laboratories reported results that were comparable to those of the control laboratories with the exception of the unsatisfactory performance of an ultra-sensitive test by one of them. Thirteen additional laboratories reported results which were satisfactory, while 22 had performances that were unsatisfactory. If we include the 10 state laboratories that did not participate in 1939 because of superior performance during 1938, we have reason to believe that a total of 26 laboratories are now performing satisfactory tests.

The 1940 serodiagnostic evaluation study will include the performances of each state and the District of Columbia laboratories, the first time this representation has been complete. The study will be conducted along the same lines as previous ones and will begin shortly after the first of the year.

FUTURE POLICIES

As more uniform standards of procedure are attained and as the level of efficiency of the participating laboratories more closely approaches that of the controls, more detailed and rigorous methods of evaluation and analysis will be essential. This will probably require the use of infected donors whose serum has a reagin content ranging in reactivity from negative to moderately positive. The selection of donors of the borderline type, however, presents very significant practical difficulties which have forced into consideration the feasibility of using an entirely different method of conducting evaluation work. This involves the use of lyophilized specimens. Experiments as to the practical use of this substance are now being performed.

Under the provisions of the Venereal Disease Control Act of 1938 the use of Federal funds to provide special technical training in various fields has been made possible. Training centers for serologists in the laboratories of the leading American serologists were already in existence and an effort has been made to stimulate their use to a greater extent through the financial assistance of the Government. Provision was also made for the acceptance of trainees at the Venereal Disease Research Laboratory of the Public Health Service. Unfortunately, all of the training centers are located in the East, a circumstance which has given rise to the consideration of a plan to establish a similar center in a location which is more readily accessible to the mountain and Western states.

Although the complete program of the Committee has been in operation for only three years, there seem to be definite indications that the approach to the problem has been a helpful one. All who engage in serologic work realize the need of cross-checking results under controlled conditions with other laboratories doing the same technical procedure. The annual survey presents an opportunity of this type, not entirely satisfactory at this time, but constituting a definite step in the right direction and forming a foundation upon which a more comprehensive system can be erected.

Up to this time the work in the evaluation of serologic tests has been only quasi-official. At the recent Conference of Laboratory Directors and Serologists held at Hot Springs, Arkansas, a recommendation was favorably acted upon which requested that the Surgeon General assume this activity as a function of the Public Health Service. This plan has been adopted by the Surgeon General and the Conference of State and Territorial Health Officers. It will go far toward placing a needed and helpful facility upon a more permanent basis.

In addition to continuing the evaluation work, the new facility should conduct, or sponsor, a broad program of research along lines which are indicated by our present rather vague general knowledge of many of the phases and factors which are involved in the serodiagnosis of syphilis. The agency could also well serve in the close scrutiny of new test procedures which are being proposed at a rate of about one each year. In the matter of standardization of test material, the dissemination of pertinent literature, and the promotion of a more widespread use of serologic examination in uncovering cases of syphilis, such measures would undoubtedly contribute definitely toward the furtherance of the general control plan.

CONCLUSIONS

(1) In the 1938 study, none of the control serologists reported a single instance of a false positive or a false doubtful reaction.

(2) In four years there have been but four false positive reports submitted by the control serologists.

(3) The "horizontal method of analysis" is very valuable in comparing the efficiency of performance of serologic tests.

(4) Many unsatisfactory results in serologic examinations are due to reliance upon obsolete technics or to short cuts; the more closely the latest technics of the author-serologists are followed, the better the results.

(5) One-fourth of the state laboratories are doing superior work.

(6) Whereas 30 state laboratories were classed as unsatisfactory in 1938, only 22 were unsatisfactory in 1939.

(7) The state laboratories are striving hard to improve their work. It is the duty of every physician to aid them as far as possible.

BIBLIOGRAPHY

1. Cumming, H. S.; Hazen, H. H.; Sanford, A. H.; Senear, F. E.; Simpson, W. M.; and Vonderlehr, R. A.: The Evaluation of Serodiagnostic Tests for Syphilis in the United States. Ven. Dis. Inform., **16**:189 (June) 1935. Also J.A.M.A., **104**:2083 (June 8) 1935.
2. Parran, Thomas; Hazen, H. H.; Sanford, A. H.; Senear, F. E.; Simpson, W. M.; and Vonderlehr R. A.: The Efficiency of State and Local Laboratories in the Performance of Serodiagnostic Tests for Syphilis. Ven. Dis. Inform., **18**:4 (Jan.) 1937. Also Amer. Jour. Pub. Health, **27**:15 (Jan.) 1937.
3. Parran, Thomas; Hazen, H. H.; Mahoney, J. F.; Sanford, A. H.; Senear, F. E.; Simpson, W. M.; and Vonderlehr, R. A.: A Comparative Study of Serodiagnostic Tests for Syphilis as Performed by Thirty-Nine State Laboratories. Ven. Dis. Inform., **18**:— (Aug.) 1937.
4. Senear, F. E.: The Relative Value of Doubtful Reports in Conducting Evaluation Studies of Serodiagnostic Tests for Syphilis. Supplement No. 9 to Ven. Dis. Inform., p. 52, 1939.

DISCUSSION (*Abstract*)

Dr. Arthur G. Schoch, Dallas, Tex.—I am honored to be asked to open a discussion so profound and complete as this one is; consequently rather than reflect a few of my own opinions, I have collected some additional data which have a bearing on three of these five standard tests done in parallel at the Dallas Syphilis and Venereal Disease Clinic.

In the serology laboratory associated with the Dallas Syphilis and Venereal Disease Clinic the Kolmer-Wassermann, Kahn and Kline tests have been routinely carried out on all patients with syphilis. I subjected to critical analysis reports on 5,396 blood sera. The diagnosis was not made by blood serum tests alone, but as a result of careful history and physical examination. Blood and spinal fluid tests were carried out by competent observers. All history and physical examinations were done by especially trained young physicians, taking their service in this department, and in the main all patients were seen by consultants, three in number, all of whom have qualified with certification from the American Board of Dermatology and Syphilology.

From this study of over 5,000 blood sera I can state that 25.9 per cent of all sera examined gave a positive reaction with the Wassermann, Kahn and Kline tests, and 43.7 per cent negative. The remainder of 30.4 per cent showed some evidence of positivity or reagent content when examined by the method described above. The group comprising the 30.4 per cent, which could be classified as showing neither a positive nor a negative reaction in all tests, was subdivided into fifteen different groups. One of these fifteen groups consisted of blood sera which yielded a negative or doubtful reaction with all three tests run in parallel. This group made up 8.7 per cent of the entire number.

In comparing the efficiency or sensitivity of the three tests which have been routinely done in parallel for a number of years, I find that the Kolmer-Wassermann is credited with giving a positive reaction in 6.61 per cent of the total when the other two tests were negative or doubtful. The Kline gave a positive reaction in 4.47 per cent when the other two were negative or doubtful, and the Kahn test gave a positive reaction in 1.18 per cent when the other two were negative or doubtful. On the other hand, the Kolmer-Wassermann gave a flatly negative reaction when at least one of the other two was positive in 5 per cent, the Kahn gave a flatly negative reaction in 0.5 per cent when at least one of the other two was positive, and the Kline gave a negative reaction in 0.02 per cent when at least one of the other two was positive.

If one regards the first group of figures as indicative of relative sensitivity one would have no hesitancy in saying that the Kolmer-Wassermann was the most sensitive, the Kline next in efficiency, and the Kahn the least sensitive. If, however, one regards the next series of figures, one must credit the Kline test with the fewest number of flat failures in its sensitivity rating, the Kahn being next, and the Kolmer-Wassermann giving the poorest showing.

I next analyzed these data trying to answer the question of relative percentage of positive results had we relied on a single test. It may be noted that out of the 5,396 blood sera examined, 25.9 per cent gave a complete agreement with a positive reaction. If we add to this 25.9 per cent, the percentages in which the Kolmer reaction was positive, we see that had the Kolmer-Wassermann been relied upon the total number of positive reactions would have been 36.77. Had the Kahn only been relied upon, the percentages of positives would have been 34.9. Had the Kline test solely been used, the figure would have been 38.2 per cent. With these data in mind, one must conclude that the Kline test is the most sensitive, the Kolmer-Wassermann technic rating second place, and the Kahn test giving the poorest showing. Using three tests in parallel at least one positive reaction occurred in 47.6 per cent.

From these 5,396 blood sera, 56.3 per cent showed some evidence of reagin content, although only 25.9 per cent showed a sufficient reagent content to render all three tests positive.

To anyone interested in the clinical aspects of serodiagnosis of syphilis, these figures must have definite significance. From these data it becomes apparent that various methods of analysis of the same data would give the Kolmer-Wassermann a superior rating as compared to the Kahn and Kline tests on one hand; it would give the Kline test a superior rating if regarded in another light; and it would place upon the Kahn test the enviable position of always showing up in a favorable light under any method of critical analysis of data.

I think these data merely serve to confirm the opinion of the committee for the evaluation of serodiagnostic tests that no single test is accurate for the diagnosis or exclusion of syphilis, and that at least two of the five standard tests, and preferably three, should be done in parallel to obtain the greatest degree of accuracy of diagnosis.

Although it is imperative to have a base line of com-

parison, which the painstaking studies of Dr. Hazen and his colleagues ably furnish us, I believe that it is, furthermore, equally important for us to visualize clearly the diagnostic accuracy of our own laboratories.

If we relied upon a single serodiagnostic test for the diagnosis or exclusion of syphilis (and no first-class clinic or laboratory relies on a single test) we could accept the sensitivity figures presented by Dr. Hazen and his co-workers as final. Since the committee makes no attempt whatsoever to appraise the combined sensitivity of two or more tests in these studies, it behooves us as individual units to make these studies in our own clinic or practice.

In conclusion, I should like to offer a word of criticism as to the manner in which doubtful tests have been regarded as negative. I believe that any critical observer will agree that doubtful tests should not be considered as negative, since the profession at large does not do so and since the originators of the tests would not have their own diagnostic procedures considered in this light. I sincerely hope that the committee will find a fair and suitable place for doubtful results, whether they be reported on sera of syphilitic patients or on supposedly nonsyphilitic normal controls.

It is my own opinion that a greater penalty should be sustained by tests that give false doubtful reports on presumably nonsyphilitic sera than credit received for true doubtful reports on sera which contain syphilitic reagin.

Dr. R. A. Vonderlehr, Washington, D. C.—I have little to say except to ask that each and every one of you in your particular state and community cooperate with health authorities in improving the performance of serologic tests for syphilis.

Beginning the first of January, 1940, the Surgeon General will require that every laboratory receiving Federal funds demonstrate its ability to perform efficiently serologic tests for syphilis. It is quite conceivable, however, that a large number of local laboratories will not be reallotted funds under the provisions of the Venereal Disease Control Act; therefore, it behooves each and every one of the members of this Section interested in the control of syphilis to see that their constituted health authorities actually do develop some means whereby they can determine the efficiency of the serologic tests performed for them.

Personally I know of no way in which health departments can do this so well as by checking the results of serologic tests against donors whose condition is known. I think that, as Dr. Senear's committee reported at the assembly in Hot Springs last year, it is necessary that we have at least 100 donors who are normal and as far as we can tell nonsyphilitic. We are using in that particular group medical students and nurses. We tell them what we want the specimens for and they volunteer these specimens, so that those who suspect that they are infected are not embarrassed by being asked to give a sample of their blood.

In addition, at least 200 specimens of blood should be collected from patients known to have syphilis, preferably from patients in clinics operated by qualified syphilologists like yourselves. If we compile the results of these serologic tests against the clinical condition of specially selected patients in that way, I think that we can tell almost with slide rule exactness what the efficiency of the test performance is.

Dr. Hazen (closing).—I am very grateful to Dr. Schoch for bringing up the subject of doubtful tests. The committee this year decided to hit the sawdust trail of repentance after many headaches and they hereafter are going to impose a purely arbitrary reduction of one half point for each false doubtful reaction that is submitted; likewise they are going to grant a credit of one-half point for every doubtful report submitted in a syphilitic. As I say, that is a purely arbitrary arrangement. It is one that is going to be tried out to see how it works. We may change our tactics later on.

I feel it is the duty of every man present to know what his own state laboratory is doing. It is not only the duty of every man to find out what his state laboratory is doing, but it is his duty to insist that his state laboratory shall likewise evaluate the private hospital and municipal laboratories within its own domain. I wonder how many of you know how rotten the laboratories are in certain places. I know a particular laboratory, for instance, which will give the physician the record he wants upon payment of $5. If the patient has plenty of money he is only too grateful, I am afraid, at times to get a positive report and at other times, for various family reasons, he wants a negative report, and he gets it for the money. Now, a laboratory of that type certainly has no place in our world of today. If a state laboratory is bad it brings discredit upon all of us, and I think that we ought to know absolutely what our state laboratories do. I think you ought to ask your state laboratory director to tell you what his ratings are not only this year, but what they have been in the past. I am sure that he will be very happy to cooperate with you. If the state laboratory is bad today you ought to know it, so that your medical society can get after it and tell it exactly what you think of it and make it do better.

AN ANALYSIS OF PERIODIC PHYSICAL EXAMINATIONS FOR FIVE YEARS*

By J. J. BRANDABUR, M.D.
Huntington, West Virginia

In the hey-day of Greece the festivities at a Grecian banquet were ended by chanting the hymn to health, composed by Ariphron the Secyonian, as follows:

"Goddess Health, Holy Power, with you I would gladly spend the rest of my days for everything else that we value; riches, song and pleasure of love are all worthless without you. In your presence everything that one desires blooms with ease, be it ever so small; in your presence we feel free and easy, even fears leave us untouched; in your presence we are kings."

This incantation, however, seemed to satisfy the question of health so far as the Greeks were concerned in that they did very little in a positive way to sustain good health according to his-

*Read in Section on Railway Surgery, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939

tory, and this was probably because they left it entirely to the Goddess of Health. If they had done more, they might still be a ruling nation.

This is a far cry from the more practical attitude we have of maintaining health through methods of prevention: first, in the control of the communicable diseases, which has been a most important factor in increasing longevity, and now through the medium of the periodic physical examination, so much so, that the wonders which the medical profession has brought about in the diagnosis and treatment of disease give hope that a time may come when the physician will be able to analyze most illness as soon as it starts, and cure it before damage has taken place. How soon this golden age of healing will arrive depends upon the collaboration between research workers and those who work in the sciences on which medicine depends.

Nowadays we spend more time and effort preventing disability than we do in repairing damage already done. This is true, more particularly in industry where it has been found, for example, that absenteeism due to sickness, on the average, amounts to ten days per year per employee. Occupational diseases and accidents cause less than one-half of these ten days of absence. In other words, ordinary disease, such as prevails in any community, is responsible for nearly twenty times as much loss of time as trade hazards and industrial accidents combined, so that today industrial practice consists of 60 per cent medicine and 40 per cent surgery. This is particularly true of the railroad surgeon, so that his work has been broadened from the traumatic to the medical phase. The interests of the company and the employees are correlated. Since physical fitness determines accidents, therefore, industry uses it as a method of self-protection. Finally the traveling public appreciates the efforts made to guide it on a safe journey. With this knowledge, your industry has come to a full realization that something must be done in this regard, and in a great number of instances it has instituted the periodic physical examination as one of the steps of prevention.

That this is a matter of public health is demonstrated by Sayers,[1] who defines industrial hygiene as the science of the preservation of the health of workers. This science is not only a matter of postponing mortality; preventing sickness and opposing disease, but of advancing and developing physical fitness and well being; so that we pay attention not only to man's actual ailments and disease, but to conditions making for a maximum degree of personal health. The periodic physical examination is a move toward this final objective because, after all, the primary purpose of such an examination is to protect the personal welfare of each and every employee by finding out whether he has average good health, and if he is below par, advising him of any defects soon enough for correction of them, and in such a manner that the advice given to him will not be a cause for alarm.

With this thought in mind, it was considered worth-while to analyze our results for a period of five yearly periodic examinations.

We cannot measure the value of experienced eyes, but industry has come to realize that the most competent and trustworthy employees are men past 40 years. Very recently it has also been found that the man past 40 is less liable to injury, because of his acquired training and experience; so from an economic standpoint, the training of new men in skilled accomplishments is expensive and it is cheaper for the employer to keep the older men in good health and thereby keep them at work than it is to undergo the expense of turnover with its resultant upheaval and disaster. This probably accounts for the fact that the industrial surgeon's work today is more concerned with the medical than the surgical aspect. Of the 2,106 men whom we are reporting as examined in 1934, 1,700, or about 80 per cent, were over 40 years of age.

"The act of growing old graciously," says Willius,[2] "is not spontaneous, but requires deliberate preparation and the conscientious practice of a modified scheme of living. In the normal human being the curve of capability rises steadily until the greatest height is reached at about the age of 50; the individual maintains this optimum level of capability for a decade at the most, and then the phase of declivity sets in."

Our experience has been that the most of our serious breakdowns are between the ages of 45 and 55 years of age, but the significant part of this finding is that this is the time when these men are the most important factors to their families from an economic standpoint.

The constant physical and emotional strain of this generation makes demands which former generations did not have to undergo. It demands, for example, a maximum load function of the heart at all times. Little wonder, then, that the heart is frequently played out at 40, and that we find our serious breakdowns just when an employee needs to be at his best. The person who would grow old and remain sound in every respect must fit his activities to his

changing physiologic capabilities, and there is no better means of doing this than through the medium of the periodic physical examination.

In order to evaluate the good results that may be accomplished we must bore you with figures. The first analysis we shall make, therefore, takes all the major defects as a whole, and we are making a comparison of the findings in our first examinations in 1934 and the fifth examination in 1938.

In view of the fact that this is a compulsory examination, and not a voluntary one, we, of course, are dealing with the employee in average health who does not come to us with any definite complaints, but on the other hand attempts to hide them. We shall confine our discussions to the more commonly encountered defects rather than rare pathologic entities. The examinations are made by about fifty different doctors all along our system, and not by one man, so for the purpose of statistical study we have reports which are fairly well averaged and not in any way colored to prove a pet theory. It is important to state that the information secured on any examination is a matter of strict confidence between the medical department and the employee, and for that reason the reports are sent to our office only. No information is sent to a supervisory officer, except that the man is qualified or not qualified for his particular duty. Since these examinations are for the benefit of the employee primarily, a man is removed from service only when he is a danger to the public or those working with him, or if he is a danger to himself.

The ages of this particular group, which includes the engineers and firemen, range from 25 to 75 years, and are distributed as follows:

Table 1

Age of Men	Number of Men Examined	
	1934	1938
25 to 35	132	67
35 to 45	649	574
45 to 55	773	828
55 to 65	431	536
65 to 75	121	109

In 1934, we had 132 men from ages 25 to 35 and in 1938, we had 67 men in this range; in the 35 to 45 bracket there were 649 in 1934, as against 574 in 1938; in the 45 to 55 range there were 773 in 1934, against 828 in 1938; in the 55 to 65 year class there were 431 in 1934, against 536 in 1938, and the last class, 65 to 75, had 121 in 1934, against 109 in 1938. Since this is a survey over five periodic examinations, you will note an increase in the ages of the upper brackets until the last, where we note a decrease due to the fact that in this group most of the men are eligible for pension. They, therefore, leave service and we have no further record of them. The ages, therefore, as you can see, strike a fair average for the railroad employee.

In order to be fair in any analysis one must record favorable, as well as unfavorable opinions, and we shall take this into consideration. In the list of defects discovered the following was noted:

Table 2

Defects	1934		1938	
	No.	Per Cent	No.	Per Cent
Overweight	277	13.1	116	5.5
Teeth (pyorrhea, dead teeth)	317	15.0	162	7.6
Tonsils	83	4.0	10	0.5
Glycosuria	33	1.5	33	1.5
Albumin	139	6.6	32	1.5
Hernia	79	3.7	30	1.4
Abnormal heart	99	4.7	78	3.7
Blood pressure above normal	421	20.0	268	12.6

There were 277, or 13.1 per cent, overweight in 1934, against 116, or 5.5 per cent, in 1938. Whilst there may be a tendency to overlook overweight in most examinations in private practice, we consider it of importance because of its influence upon individuals with high blood pressure, and the predisposition of obese people to develop diabetes, also because the heart, kidneys and liver are prematurely exhausted due to the extra work placed on them by the body when it is carrying excess fat.

"Focal infection as an etiologic factor of general disease is now an established pathological principle," according to Billings, and in case we are wont still to doubt this saying, Bierring[3] helps to settle it as follows:

"In spite of the critical attitude maintained in certain quarters regarding the continued acceptance of the concept of focal infection, it should be acknowledged that the efforts that have been proposed to detect and then to obliterate all forms of focal infection in the mouth and throat, as well as elsewhere in the body for preventive as well as curative purposes, besides being in accord with sound reasoning from general principles,

has received the support of strong experimental evidence."

Since these men do not come to us for a cure, we class our findings in the preventive field and feel that we have accomplished a purpose, because in 1934 there were 317 men, or 15 per cent, with dental sepsis, in the form of pyorrhea or dead teeth, and this figure was reduced to 162, or 7.6 per cent, in 1938. Under throat infections we had 83, or 4 per cent, with diseased tonsils, and this figure was reduced to 10 or 0.5 per cent, in 1938. In spite of the fact that this is mostly preventive work, we have at the same time encountered several who have been helped considerably in arthritic conditions following the removal of teeth and tonsils, and one very interesting case of chorioretinitis in both eyes, which was apparently cured following the removal of diseased tonsils. Certainly these cases alone demonstrate that we are attempting to advance and develop physical fitness and well being by increasing the efficiency of the human body, because in the last case the man would certainly have lost his vision and with it his efficiency.

That our employees are more health-conscious is evidenced by their inquiries in these examinations with regard to sugar in the urine. Whether this is due to the prominence which is being given to diabetes in certain lay magazines is a question. Nevertheless, it shows that it is an important phase of the examination, and no routine examination is complete without it. This is particularly important in our examinations, because we are dealing with men whose judgment cannot be altered by the fact that they are carrying an excess of sugar in their system. In 1934, there were 33 cases with glycosuria, and in 1938 we found the same number of cases. We think that we have found these cases in the very early stages, because at present there is not one who needs insulin therapy. Our results with regard to the detection of early kidney disturbances have made us realize the importance of a complete urinalysis. In 1934, there were 139 cases, or 6.6 per cent, with traces of albumin in the urine, and this was reduced to 32, or 1.5 per cent, in 1938. Because of these findings we were able to discover a number of other abnormal genito-urinary conditions, such as enlarged prostate and several bladder tumors in their incipiency. Since a routine prostatic examination is not made by all of the doctors on our system, we are unable to give you any data in this regard.

All employees must be stripped for examination. The strictest privacy is observed by the physician, so that no two men are examined in the same room at the same time. The reason for complete exposure is that it immediately reveals any deformities or defects which the employee will invariably hide, and this is particularly true of hernia. In 1934, there were 79 hernia cases, or 3.7 per cent, and in 1938 there were only 30 cases, or 1.4 per cent.

Many men who continue their activities into the sunset years of their lives at the same high level which characterized the daily program of youth and early middle age are cut down without warning as some vital structure suddenly rebels at the demands it can no longer meet. Particularly is this true of the heart, and a great deal of the objection to the periodic examination is that many a man, soon after his heart has been examined by a physician and found to be all right, has suddenly been invalided by a cardiac accident. Our answer to this is, first, that we must make an inspection of our engines, trains and tracks, yet unfortunately it so happens every once in a while that following an inspection we have an accident. That does not necessarily mean that inspections of equipment should be discontinued. Why, then, should we discontinue the examination of the man behind the equipment because of an occasional cardiac accident which is unpredictable? Secondly, we now know that the history of the man's subjective complaints is just as important in regard to the heart as the examination and we have tried to impress our examining surgeons with this thought. We find that in 1934 we had 99 men with abnormal heart action, and in 1938 only 78. This includes tachycardia, arrhythmia and other minor heart defects, as well as the major findings. This is a phase of the examination regarding which the employee is very apt to attempt to conceal his complaints because he fears for his job. If the examining physician takes time to explain that he is interested primarily in prolonging the man's life so that he may enjoy it in comfort by averting or postponing a cardiovascular accident, the employee will often volunteer information which is important.

Because of the advances in medicine, particularly the increasing span of life due to prevention of contagious diseases, the number of cases of hypertension are naturally on the increase. It is primarily an ailment of middle life and old age, but the etiology is still very obscure and

highly controversial. Various factors play a role; psychic and nervous disturbances, so-called high pressure living, derangement of the internal secretory mechanism, absorption of exogenous and endogenous poisons, hereditary predisposition, and lastly, as Goldblatt's[4] experiments have shown, hypertension may be due to pathologic changes in the kidney. All in all, the problem is a confusing one, and the results of our examinations make it more confusing.

Table 3

NUMBER OF MEN WITH HIGH BLOOD PRESSURE

Number showing high blood pressure in 1934	421
Number disqualified or deceased since 1934	71
	350
Number examined since 1934 with high blood pressure	32
	382
Number examined in 1938 showing high blood pressure	268
Number of blood pressures reduced to normal	114

In 1934, 421 men, or 20 per cent of all men examined, had what we term abnormal blood pressure, and this figure was reduced to 268, or 12.6 per cent, in 1938. Since this report covers a period of five examinations, obviously a certain number of these men are deceased, and a certain number have been removed from service, so we no longer have any record of them. In order to see whether this might be the reason for the apparent reduction, we analyzed these cases very closely. In 1934, there were 71 men who had high blood pressures who are now deceased or who have been removed from service. Subtracting these 71 from the 421 men who in 1934 had high blood pressure, we have 350 who are still accounted for. On the other hand, since in a period of five years we are bound to note some increases in pressure, we found that 32 men who in 1934 had normal pressures now have abnormal pressures. Adding these 32 men to our 350 still accounted for, we have 382 to balance the roll. As there are only 268 who still have abnormal blood pressure, we feel that since 1934 there has been a reduction to normal in 114 cases.

We then thought that in view of Goldblatt's work it might be interesting to find out how many of the cases of abnormal blood pressure had signs of kidney disease as evidenced by a trace of albumin.

In 1934, there were 71 men, or 3.3 per cent, with abnormal blood pressure who had albumin in the urine and 20 men, or about 1 per cent, in 1938. There is a definite increase in the number with albumin and high blood pressure after 45 years of age from 7 to 19, and from 19 to 31 between the ages of 55 and 65. But in analyzing this factor more closely, we found 58 men, or 2.7 per cent, who had normal blood pressure in 1934 who also had albumin in the urine, and in 1938 there were 10 men, or 0.5 per cent. Here, even though these cases at present show normal blood pressure, we note an increase in a different age group, namely: in the 25 to 35, we have 5 cases with albumin, whereas we had none in this age with the high blood pressure group, and we have an increase in the 35 to 45 age group to 25 men, or our greatest number of cases with albumin. This is decreased to 16 cases at ages between 45 and 55, and 8 in the 55 to 65 bracket. Are these potential hypertension cases? It certainly will be interesting to follow them through our periodic examination.

Since age is apparently a definite factor in hypertension, we further analyzed these cases into age groups with the following findings as noted in *Table 5*, where we noted both the systolic and diastolic abnormalities.

You will notice that there is a definite increase to 35.7 per cent from 55 to 65 years of age as one would expect. But the rise begins to be evident between 45 and 55 years of age, and

Table 4

CASES WITH ALBUMIN

	Hypertension with Albumin		Nor. Blood Pressure with Albumin	
Age of Men	1934	1938	1934	1938
25 to 35	0	0	5	0
35 to 45	7	1	25	5
45 to 55	19	5	16	3
55 to 65	31	11	8	2
65 to 75	14	3	4	0
	71	20	58	10

Table 5

AGE OF MEN WITH HIGH SYSTOLIC PRESSURE

Age Years	No. of Men Examined		No. and Per Ct. Found with High Systolic Pressure			
			1934		1938	
	1934	1938	No.	Per Ct.	No.	Per Ct.
25 to 35	132	67	12	9.1	1	1.5
35 to 45	649	574	72	11.1	44	7.7
45 to 55	773	828	162	20.9	90	10.8
55 to 65	431	536	154	35.7	115	21.5
65 to 75	121	109	38	31.4	18	16.5

this is the age where we note our greatest number of breakdowns.

Our standard for determining a case of abnormal systolic blood pressure is found by adding 85 to the age of the patient, as we have found that this fits in with the normal in a better way. Following this idea the list of systolic pressures ranged as follows:

Table 6

SYSTOLIC BLOOD PRESSURES ABOVE NORMAL

Ranging from	1934	1938
140 to 150	39	13
150 to 160	106	72
160 to 170	99	93
170 to 180	82	56
180 to 190	36	16
190 to 200	23	12
200 to 210	16	4
210 to 220	10	2
220 to 230	6	0
230 to 240	3	0
240 to 250	1	0
	421	268

This table shows us that most of the cases in which further destructive changes may be prevented lie between 150 and 180. You will also note that we have no cases above the 220 range in 1938. This is explained by the fact that we have removed these men from service.

We consider any diastolic pressure of 100 or over as abnormal.

Table 7

DIASTOLIC BLOOD PRESSURE ABOVE NORMAL

Ranging from	1934	1938
100 to 110	88	53
110 to 120	44	27
120 to 130	14	7
130 to 140	4	2
140 to 150	3	0
150 to 160	2	0
160 to 170	1	0
	156	89

Here we note that in 1938 we have no cases above the 140 range. The reason is probably because these men have either died or have been removed from service.

In *Table 8*, the distribution of the diastolic blood pressures shows a very evident rise in the ages between 45 and 55, with a still greater increase between the ages of 55 and 65. We also noted here that the decrease between 1934 and 1938 was not so great as in the systolic pressures. Does this mean that we can place more significance upon an abnormal diastolic pressure?

Finally, we are interested in the question of treatment of these cases because a definite improvement is shown, as you have noted from our figures. Naturally since these groups of men are spread over an area covering thousands of miles all along our line, they were referred to various physicians and there was evidently no specific form of therapy introduced, because in the usual letter that we received from the physician taking care of these men the statement was made that the physician had placed the employee upon a diet and under frequent observation and advised him to relax and free himself from worry. In other words, the men are being taught the extent of their physiologic capabilities and how to keep themselves in the best of health.

With the tendency to specialization in medicine becoming more pronounced, a neurologic examination seems to be difficult, but, strictly speaking, is easy; and whilst the neurologic problems as a whole are under the domain of the neurologist, nevertheless we are concerned with them in railroad work because we are dealing with men who must constantly be on the alert mentally at all times. They are a potential danger or hazard if they are stupid, dull or emotionally unstable. A complete history oftentimes reveals that employees are trying to get by in an examination by failing to make known some definite disability, such as epilepsy or tabes in its early stages. A history check-up into vasomotor changes such as polyuria, tachycardia and other nervous manifestations may reveal defects. A complete inspection for other nervous findings such as whether the gait is spastic, ataxic or hemiplegic, tremors, or involuntary movements, and finally, an ophthalmoscopic examination may reveal evidence of importance. The cranial nerve check-up

Table 8

AGE OF MEN WITH HIGH DIASTOLIC PRESSURE

Age Years	No. of Men Examined		No. and Per Ct. Found with High Diastolic Pressure			
			1934		1938	
	1934	1938	No.	Per Ct.	No.	Per Ct.
35 to 45	649	574	16	2.5	9	1.6
45 to 55	773	828	51	6.6	22	2.6
55 to 65	431	536	62	14.3	48	9.0
65 to 75	121	109	27	22.3	10	9.0

may show Argyll-Robertson pupil, which is not necessarily luetic, but may be present in multiple sclerosis, encephalitis and chronic alcoholism. The deep tendon reflexes also tell us a story. To prove further that the neurologic examination is not only a part of the railway surgeon's duty, but that the examining physicians on our system realize the importance of it, is well evidenced by the fact that we have detected several cases of neurologic significance by these simple routine tests. These include brain tumors, epilepsy, tabes dorsalis, pernicious anemia with cord changes, encephalitis, and toxic goiter.

We have thus attempted to place before you the results of our periodic examinations over a five-year period to show you how we are trying to secure the aim of public health in industry by making the average individual more health-conscious, and this does not apply only to older individuals. Younger persons who we find, through these examinations, are living beyond their capabilities may be taught to make adjustments at an early age. Thus we may avert or at least postpone a large percentage of the cardiovascular accidents that are responsible for most of the early tragedies of life and place an economic burden on the surviving members of the family. In older persons the periodic physical examination presents an opportunity to stress the fact that in all of us a change is bound to take place. This varies with different individuals, but occurs, nevertheless, and it is important for them to know that by decreasing loads of all sorts; by learning to take frequent periods of rest and relaxation; by arranging for frequent systematic intervals of recreation, they may look forward to their days of regression with a feeling that they may enjoy the sunset years of life rather than look at them as a period of invalidism. How many men do you know of venerable age who have been under your medical care for a period of years who are still not only enjoying life, but are also contributing to it to the utmost? This is the aim which we are trying to accomplish, and if we have done nothing else but teach these men how to live properly and in this way to preserve their health, we feel that we have done something in a constructive or positive way rather than intoning a hymn to the Goddess of Health as was done by the Greeks.

REFERENCES

1. Sayers, R. R.: Public Health Aspects of Industrial Hygiene. J.A.M.A., **111**:679 (August 20) 1938.
2. Willius, F. A.: Proc. Staff Meeting, Mayo Clinic, **14**:41, 1938.
3. Bierring, Walter L.: Focal Infection. J.A.M.A., **111**:1421 (Oct.) 1938.
4. Goldblatt, Harry: Studies on Experimental Hypertension. Ann. Int. Med., **11**:1 (July) 1937.

DISCUSSION (*Abstract*)

Dr. W. J. Lancaster, Wilmington, N. C.—I first want to congratulate Dr. Brandabur on giving us the first authentic report that we have ever had in this Section on periodic examinations from a railroad standpoint. The value of periodic examinations is not confined entirely to any one set of individuals or corporations. The value to the railroad has been brought out very nicely, in that it keeps men who are adequately trained on duty. From a railroad standpoint that is an economic situation. From the standpoint of the physical well-being of the patient himself, it produces a longer and happier life. From the standpoint of the public, we, the doctors, should exert all the effort that we can put forth to see that the employees, particularly those in responsible positions, are physically and mentally capable of carrying out their responsibility from a public safety standpoint. The cost of these examinations is rather large, but statistics like Dr. Brandabur's are valuable.

His organization, I think, pioneered in making periodic examination of employees. These examinations run into a cost of approximately $25,000 a year to the corporation making them, of course depending more or less upon the number of employees and the distances between the various points on the line. But statistics have shown that it is money well spent.

The railroad surgeon, using an expression that a previous railroad surgeon employed, used to be known as a kind of necessary evil, something that the company had with it, that it did not know what to do with and did not know how to get rid of.

That era has passed and the railroad surgeon today is recognized by the executives of the organizations as an essential factor in the running of that organization, in keeping it going, in its defense.

An important thing that I think this periodical examination will show is the diseases predominating in different sections of the country. In the South particularly, due to the negro labor, there are the predominating syphilis and tuberculosis, both of them wasting and tearing down diseases and both of them incapacitating diseases. In certain other sections where that class of employee is not used they do not run into the same numbers.

We thought enough of this need on our railroad, after a rather exhaustive study, to put in periodic examinations. We are getting good results with them, and good cooperation from the employees, and we fully believe that we are carrying the examinations out primarily for the good of the employee himself; secondarily for the good of the corporation; and thirdly for the good of the public at large. Along the lines suggested by the American Medical Association, the American College of Surgeons and the American Hospital Association, we are trying to keep good, accurate records. The methods required by these organizations provide standards.

These examinations and records are essential not only in railroad circles, but in our general work.

Dr. George A. Traylor, Augusta, Ga.—It is not difficult to argue for the desirability of periodic and pre-

employment physical examinations of all employees in railway service. Mechanical equipment is inspected before being sent on a run and reinspections are made at junction and other points. Nevertheless, with the most careful supervision accidents will sometimes occur. No one will attempt to deny the necessity for roadbed, rolling stock and trackage and their upkeep. A well-trained employee has indisputable value, and his periodic physical overhauling is just as necessary for the safe transit of trains as is that of rolling stock and roadbed.

Most railway employees enter service when young, but are as subject to degenerative diseases as others of the population. Frequently the detection of an incurable malady in its inception offers an opportunity for amelioration or placement in a position where less wear and tear and responsibility occur.

In an analysis of 738 deaths of railway employees who had undergone periodic examinations, it was found that 366 (not quite 50 per cent) died of vascular disease; and these deaths are likely to happen while on duty in a responsible position and with many lives at stake.

Each railway system has its own files of examinations, one railroad having records of over 18,000. If the medical directors and chief surgeons of the various railroads would, in conference, suggest standardized procedures and nomenclature, so that results could be compiled and studied, it would be to the advantage of the railroads as well as the population in general.

Dr. Brandabur (closing).—I am associated with a doctor who has charge of another railroad in which periodic examinations of about 15,000 employees have now been completed. The result of their check-up practically coincides with the results of our examinations, showing that the periodic examination is of very definite benefit.

THE TREATMENT OF TYPHOID FEVER BY THE THIAZOLE DERIVATIVES OF SULFANILAMIDE*

A PRELIMINARY REPORT OF FOUR CASES

By J. O. WEILBAECHER, JR., M.D.
EMMA S. MOSS, M.D.
HENRY M. TAYLOR, M.D.
and
HOMER DUPUY, M.D.
New Orleans, Louisiana

The development of the newer thiazole derivatives of sulfanilamide and the demonstration of their bacteriostatic action on *E. typhi in vitro*[1] would seem sufficient justification for a determination of their possible clinical value. In this preliminary report are set forth the results of this type of therapy in four proven cases of typhoid fever.

*Received for publication April 5, 1940.

*From the Departments of Medicine and Pathology of Charity Hospital of Louisiana at New Orleans and the School of Medicine of Louisiana State University.

CASE REPORTS

Case 1.—L. D. (I-40-354), a colored male 14 years of age, was admitted to Charity Hospital of Louisiana at New Orleans January 3, 1940. For 14 days he had had vague abdominal pain and distention, associated with diarrhea, anorexia and fever. At the time of admission the temperature was 103° F., the pulse rate 110, and the respiratory rate 30 per minute. He was markedly dehydrated and acutely ill. Physical examination was negative otherwise except for mild generalized abdominal tenderness; the spleen was not palpable. Urinalysis was negative and the red and white blood cell counts were within normal limits.

On the third day of hospitalization, after the diagnosis of typhoid fever had been established by blood culture, treatment with sulfamethylthiazole was instituted. On the morning of the fourth day the temperature, which had varied from 102 to 104.8° F., dropped to 99.4° F. A rise to 104.8° F. that afternoon, together with a slight chill, was later regarded as the reaction to an intravenous infusion of glucose solution. On the second day of treatment (the fifth day of hospitalization and the nineteenth day of illness) the maximum temperature was 99.8° F. On the third day of treatment the maximum temperature was 101.6° F., and on the fourth day the maximum was 99.6° F. (*Fig. 1*). Thereafter the temperature was normal until discharge January 24, 1940.

The initial dose of sulfamethylthiazole was 4 grams. Two grams were given every two hours thereafter except for a 24-hour period following the chill mentioned above, when the drug, because its action was not fully known, was discontinued until it was determined that the infusion was responsible for the reaction. Sulfamethylthiazole therapy was resumed in 1 gram doses every four hours for the next three days. Then, after the temperature remained persistently normal, the interval was lengthened to eight hours until January 13 (the ninth day of therapy), after which it was discontinued entirely. Daily urinalyses and blood studies did not reveal at any time any evidence of a toxic reaction to the drug. The total dosage was 58 grams.

The response to sulfamethylthiazole therapy in this instance was striking. The patient, who had been acutely ill and whose previous course had been entirely typical of typhoid fever, promptly improved. Within a few days the temperature was normal, appetite returned, the sense of general malaise disappeared, and the state of alertness, in contrast to the lethargy which usually accompanies typhoid fever, was quite remarkable. Convalescence was uneventful, and recovery was apparently complete.

Case 2.—S. C. (I-40-1351), a colored female 19 years of age, was admitted to Charity Hospital of Louisiana at New Orleans January 8, 1940. For 11 days she had had vague abdominal pain associated with fever and weakness, and at the time of admission she was in a toxic stupor and seemed critically ill. The tempera-

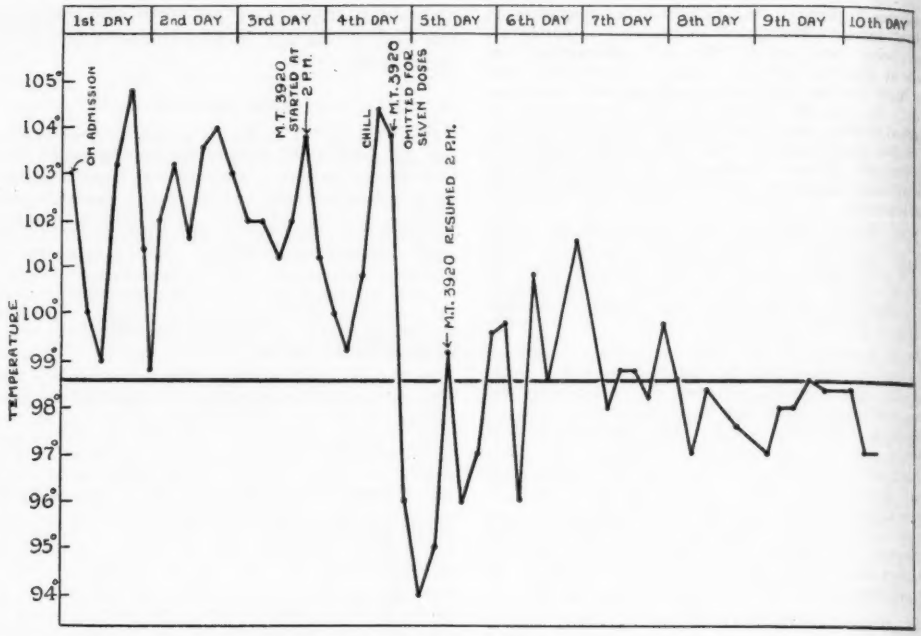


Fig. 1, Case 1
Temperature Chart. M. T. 3920=sulfamethylthiazol.

ture was 104° F., the pulse rate 136, and the respiratory rate 30 per minute. Physical examination was negative except for the general appearance, slight diffuse abdominal tenderness, and the presence of a palpable spleen. The red blood cell count was 3,400,000 and the white cell count 10,000 per cu. mm. The proportion of polymorphonuclear leukocytes was 76 per cent.

The clinical findings were entirely in keeping with a diagnosis of typhoid fever, which was further supported by the patient's place of residence. Treatment with sulfamethylthiazole was therefore instituted without waiting for the blood culture to be reported; on the following day the diagnosis was verified by the growth of *E. typhi.*

Because of the patient's critical condition an initial dose of 2 grams of sulfamethylthiazole was given and the same dose was repeated every two hours for four days. Every precaution was taken to anticipate any possible toxic effect from this massive therapy, and clinical observation and daily blood studies and urinalyses at no time revealed any untoward results. At the end of four days the patient became alert and responsive and her appetite was greatly improved. The temperature had gradually fallen to 99° F. and the pulse rate had slowed from an average of 145 to an average of 115 per minute.

At this time the dosage was reduced to 1 gram every four hours. The pulse rate remained between 100 and 120 per minute and the temperature between 99° F. and 102.8° F., and January 18 (the eleventh day of therapy and the twenty-second day of illness) the dosage was again increased to 2 grams every four hours. The temperature was subnormal for 36 hours, then gradually rose to a maximum of 101.4° F. At this time a gluteal abscess which had been forming ruptured spontaneously, whereupon the temperature fell to normal and there were no further elevations. The patient was discharged, apparently entirely well, February 16, 1940. The total dosage of sulfamethylthiazole was 118 grams.

This patient's response to sulfamethylthiazole was somewhat less rapid than the response of the first patient, but she was more seriously ill and the clinical improvement, even though the temperature elevations persisted, was striking.

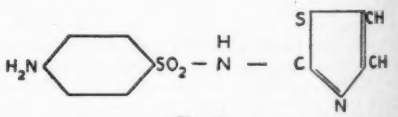


Fig. 2
Sulfathiazol.

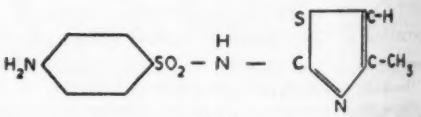


Fig. 3
Sulfamethylthiazol.

It seems logical to assume that the infection in the buttock was at least partially responsible for the obstinate fever.

**Case 3*—A. Z. (T-40-2762), a white male 28 years of age, was admitted to Charity Hospital of Louisiana at New Orleans January 6, 1940. For seven days he had had a headache and fever, and diarrhea had been present for three days. At the time of admission the temperature was 104° F., the pulse rate 88 and the respiratory rate 20 per minute. The patient was acutely ill. He was moderately obese. Physical examination revealed questionable rose spots over the anterior chest wall, but was otherwise negative. The spleen was not palpable. Urinalysis was negative. The red blood cell count was 4,500,000 and the white cell count 9,700 per cu. mm. The proportion of polymorphonuclear leukocytes was 70 per cent. The blood culture was positive for *E. typhi*.

Sulfamethylthiazole therapy was begun two days after admission in the dosage of 2 grams every four hours. At the end of 24 hours it was discontinued because of the appearance of bloody stools. Three days later sulfathiazole therapy was begun and was continued in the dosage of 2 grams every four hours for five days. The temperature during this period varied between 100.6° F. and 103° F.

For the next five days sulfamethylthiazole was administered in the original dose. At the end of this time the development of a morbilliform rash and a fall in the red blood cell count to 2,900,000 per cu. mm. necessitated the discontinuance of the drug. In all, 29 grams of sulfathiazole and 55 grams of sulfamethylthiazole had been administered.

The rash disappeared promptly after the drug was discontinued, but the temperature curve continued as before, the elevations finally ending February 11, 1940. At this time the red blood cell count was 4,400,000 per cu. mm. and the white blood cell count 7,700. The patient was discharged, apparently well, February 24, 1940.

From the standpoint of drug therapy this case must be regarded as a failure, although the total amount administered was very large. Administration was irregular, it is true, due to the appearance of bloody stools, but at no time was there an improvement in the fever curve and the definite clinical improvement noted in the first two cases reported was never apparent. The mild anemia and the toxic morbilliform rash observed were probably the result of the drug, for both disappeared when the therapy was discontinued.

Case 4.—L. S. (I-40-7238), a white male 17 years of age, was admitted to Charity Hospital of Louisiana at New Orleans February 10, 1940. For 10 days he had complained of fever, with occasional nausea and vomiting. He appeared acutely ill and lethargic, and at the time of admission the temperature was 104.6° F., the pulse rate 100 and the respiratory rate 30 per minute. Physical examination revealed rose spots on the anterior chest wall and abdomen, and a mild generalized abdominal tenderness. The spleen was not palpable. The red blood cell count was 4,500,000 and the white cell count 6,400 per cu. mm. The proportion of polymorphonuclear leukocytes was 60 per cent. Blood culture revealed a growth of *E. typhi*.

Sulfamethylthiazole therapy was immediately begun, 2 grams being given every four hours for six doses. At the end of this time the dosage was reduced to 1 gram every four hours. On the fourth day after treatment was begun the clinical improvement was striking. The patient was alert and responsive, and the appetite was much better. The temperature, which had fallen to 99° F., rose irregularly in the evening for the next six days to a maximum of 102° F., but convalescence thereafter, with that exception, was without event. February 27 the dosage of sulfamethylthiazole was reduced to 1 gram twice a day, and none was given after March 5. The total dosage was 96 grams. The patient was discharged, apparently well, March 7, 1940. Daily urinalyses and blood counts revealed no toxic reaction to the drug.

It is felt that the response of this patient to sulfamethylthiazole therapy was just as striking as the response of the patient upon whom it was first tried (*Case 1*).

COMMENT

Although there was definite improvement following the administration of sulfamethylthiazole therapy in two of the cases (*Cases 1* and *4*) reported herewith, and more indefinite improvement in a third case (*Case 2*), the therapeutic value of this drug can be established only after further and far more extensive observation. On the other hand, in these cases, although the temperature curves did not fall very rapidly, there was a uniform clinical improvement in all three patients who exhibited any response, and the length of the illness was shortened considerably from the four- to eight-week course observed in patients treated by the ordinary measures. The other patient (*Case 3*) did not respond at all. There was no mortality in these cases, and no complications occurred, but definite statements on these points can be made only after further observation in larger series.

The optimum dosage of the thiazole derivatives of sulfanilamide must also be determined by further trial. It is interesting, however, to note that three of the four patients withstood massive doses without ill effects, as demonstrated by daily laboratory studies. The occurrence of slight anemia and the appearance of a rash in one case (*Case 3*) after the administration of a proportionately smaller amount of the drug than was used in the other cases emphasizes the known inability of the physician to predict the

*This case is reported through the courtesy of Dr. J. H. Musser, from the service of the Tulane University School of Medicine in Charity Hospital at New Orleans.

production of toxic effects by the use of drugs of the sulfanilamide group and makes clear the importance of using them with the greatest caution, at least for the present.

SUMMARY

(1) The results of sulfamethylthiazole and sulfathiazole therapy in four proven cases of typhoid fever are presented.

(2) The apparently good results in three of these cases seem to justify the continued trial of this type of therapy in typhoid fever.*

*The thiazole derivatives used in this study were supplied by the Winthrop Chemical Company, in whose Department of Medical Research the laboratory data were demonstrated concerning their *in vitro* effect upon the typhoid bacillus.

SOME MEDICOLEGAL ASPECTS OF ALCOHOLIC INTOXICATION*

By FERDINAND C. HELWIG, M.D.
Kansas City, Missouri

This is to be a discussion of a question which seems very, very simple, because I never met anybody who did not have an answer to it. In fact, I have heard, and dare say that everyone here has heard, about fifty answers to it, all different.

When is a person drunk?

I believe there is a correct rejoinder, and will now attempt to set it forth.

When is a person clinically and legally drunk? To begin with, the law regarding the careless and over-indulgent drinker is very interesting and at times has certain humorous angles. Thus, the legal definition of drunkenness is not always the same. Hall[1] quotes a decision from a Texas court as follows:

"It is difficult to draw the line on a drunk: there are the stages of being vivacious, foxy, tipsy and on a high lonesome. It is about as difficult to determine when a young lady gets to be an old maid as to tell when a man has taken enough alcoholic stimulant to pass the line between jolly sober and gentlemanly drunk."

Many years ago when Mr. Bowker and Mr. Moonface, two characters in a Surtees novel, were debating the question before the Sublime Society, their social club, the definition stood somewhat as follows:[2]

Mr. Bowker: "It is enacted that no human shall be considered drunk or liable to the pains and penalties contingent upon intoxication if he can lie still without holding."

Mr. Moonface: "Now after he is incapacitated from walking, if he can lie still on the floor, is he considered sober?"

Mr. Bowker: "He is not considered drunk."

On the other side we have the opinion of a medical witness[1] before a courtmartial who stated that "anyone who had taken a drink," even though it be but a thimbleful of beer, was "under the influence."

Certain phases of British law concerning drunkenness have some amusing corollaries. Thus, Dickson,[3] discussing the heavier penalties imposed on an individual when in charge of "any horses, carriage, cattle or steam engine, etc.," mentioned the amusing incident of the arrest of a circus employee who was drunk while in charge of a camel and of the soldier who was "drunk on the line of march while employed as a trombone player." In another army is the record of the colonel who had been drunk for a year. When he was tried before a courtmartial on the charge of habitual drunkenness he displayed the prescription of his physician which called for one quart of whiskey every day. Possession of this prescription was grounds for his acquittal.[4]

There are a great many variables to be considered when we, as medical men, attempt to make an unbiased decision as to whether Richard Roe, who has had a drink or several drinks, is drunk and incapable. Medical witnesses may be asked to decide the degree of influence which alcohol has upon a given individual at a given time and I will try to show later that it is sometimes a mistake to thrust such a serious burden upon a medical examiner.

Very frequently the observations of police and lay witnesses are of greater value than the medical examination in determining intoxication, since what actually happened on the spot is very important. Any data that can be obtained regarding the actions of the accused previous to the time that a diagnosis of suspected inebriation

*Read in Section on Pathology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

*Author's Note: Since presenting this paper a communication has appeared in the *Journal of the American Medical Association* for March 23, 1940, Vol. 114, No. 12, p. 1098, entitled "Chemical Tests for Alcoholic Intoxication," signed by Professor Chauncey D. Leake, Joseph B. Swim, and Elton L. McCowley, of the University of California. They discuss the 1939 report of the Committee on Tests for Intoxication of the National Safety Council and mention certain investigations which they have made that cast great doubt on the specificity and reliability of chemical tests for alcohol in the blood. It is their opinion that it is therefore unwise to recommend legislation involving such specific methods and figures.

was made may also be highly important. A physician may not see the accused for some time after the alleged legal infraction, at which time the actions of the accused, although very important, may be quite different from those manifested a half hour previously. The examining physician should carefully note the general demeanor of the suspect and it must be constantly kept in mind that there may be a striking change in his actions, dependent not only upon the time element elapsing after the alleged ingestion of alcohol, but several other factors as well may be active. Observation of the subject's attitude, such as pugnacity and sullenness, or his being bombastic or talkative, are points worthy of record. It is a well-known fact that the emotional shock attendant upon arrest may have a strikingly sobering effect, and it is not at all unusual for a thoroughly inebriated individual to appear quite sober after an accident. Such a change is possibly a purely psychic reaction which in some mysterious way produces a temporary redistribution of alcohol in the body. We all know that unusual mental and physical stimuli often will cause a thoroughly drunken man to gain sufficient control of himself to appear quite sober, in a manner perhaps similar to that which causes one thoroughly exhausted from lack of sleep to come quickly to his senses. It is, therefore, of utmost importance to observe the accused after such stimuli have been removed. I have frequently seen men in jail go promptly to sleep after being incarcerated for suspected drunkenness while at the time of arrest they seemed to be in good control of their faculties. Such a reaction is certainly unusual in one who is stone sober. Ebel[5] explains this sobering action of emotional stimulation on the basis of a release of adrenalin into the system. It is known that in adrenalectomized animals the tolerance for alcohol is markedly decreased. Moreover, even moderate indulgence in alcoholic beverages will cause splanchnic vasoconstriction with a resultant increase in the circulation of the blood in the brain while fright or high emotional stimulation will produce sudden and marked splanchnic vasodilatation which decreases the rate of flow of blood containing alcohol through the brain.

Should one suspected of drunkenness be unconscious or asleep, it is highly important to make a careful differential diagnosis between alcoholic unconsciousness and other conditions which may duplicate it. Careful scrutiny should be directed toward the subject's clothing, for any evidence of falling, tearing or any disarrangements, and he should be interrogated at once as to the reason for any such abnormality in his dress. Often the tongue of an inebriated individual is dry and furred, the breath is heavy and usually contains an odor of some alcoholic beverage. The question of odor, however, is of little significance in the diagnosis of drunkenness and has no quantitative relationship to the amount of alcohol consumed. I have frequently been unable to smell alcohol on the breath of a thoroughly drunken man. A great deal depends on the cooperation of the exhalor, nature of food consumption, particularly foods with a definite fragrance such as onions, garlic, mints, and likewise the olfactory acuity of the smeller is important. Moreover, the congenerics of the consumed beverage is much more important than the alcohol itself, since it may be impossible to smell alcohol on the breath of one who has ingested diluted ethyl alcohol free of such congenerics. The subject's character of speech and his ability to repeat certain difficult phrases may serve as corroborative evidence in a drunken suspect, especially if speech is muddled and ideas are incoordinated.

The staggering gait is classically construed as a sign of drunkenness, yet we have undoubtedly all seen markedly intoxicated individuals totally incapable of carrying on an intelligent conversation who had no difficulty in walking straight or following a straight line. This ability to "keep on their feet," so to speak, will cause no suspicion of drunkenness from observers. On the other hand, it should be stressed that unsteadiness and instability in walking may be due to a wide variety of nervous disorders. The same may be said for all the different tests for motor incoordination, yet the tests are all of some value. Such simple examinations as the finger to nose test, picking up objects from the floor, rapidly turning about, and so on, should be applied, but we must keep in mind that the only legal implication of a subject's incoordination is that he is incoordinated. Memory tests may also be tried, such as asking the name and address, the date and day of the week and questions as to what has happened during the previous hour or two.

After all such examinations, we must in all fairness remember that much leeway should be given to the subject under suspicion of drunkenness in order to give the examination proper value, since his reaction may be due solely to emotional strain. I have seen a perfectly sober

person who, under arrest, was utterly incapable of signing his own name, unable to remember his own phone number or even talk except in an excited and not thoroughly coherent manner.

From the clinical examination it seems, therefore, obvious that great care, accurate observation and a thorough knowledge of medicine are required before a positive diagnosis of borderline intoxication should be rendered. In many of those cases such a diagnosis on clinical grounds alone may be impossible.

As a result of this variation in clinical behavior, a number of chemical tests of different body fluids have been elaborated for the purpose of determining the degree of intoxication. The sputum, urine, blood, breath and spinal fluid have all been subjected to analysis and many articles have appeared in the literature in recent years which attempt to correlate the alcohol concentrations of these different body fluids with the clinical picture of intoxication.

BREATH

Recently much attention has been devoted to the determination of the quantity of alcohol in the expired air.[6] This test has been used because of the ease with which samples may be obtained and also because samples of the subject's sputum, urine, blood or spinal fluid have been objected to by some courts on the basis that such evidence could not be used in court against an accused. There are a number of objections to the breath test, since false values can readily be obtained. If a person has had a drink of alcoholic liquor within a few minutes before the breath is tested or if he has been vomiting, hiccoughing, or regurgitating following the ingestion of alcohol the result might be worthless. Nevertheless, such tests are being accepted as evidence and are being utilized by some police departments in this country. The figure, 0.15 per cent blood alcohol, is accepted by some writers as the index of intoxication. We will discuss the question of percentages later.

URINE

Chemical tests of the urine[7] have been employed and some of the same objections have been raised against this procedure as obtain for blood tests, which will be subsequently considered. It seems to me that urinalysis for alcohol may be even less satisfactory as an accurate test for degree of drunkenness than the test for the alcoholic content of the expired air, as there may be no way of determining when the alcohol present in the urine was excreted by the kidney. Moreover, the time that the sample was obtained may bear no relationship to the alcoholic brain concentration at the time of the illegal actions of the person examined. If urine is collected during the period of active alcohol absorption, naturally the blood and brain content will be higher than that of the urine alcohol, and if the sample is collected when the blood alcohol level is falling there may be an increase in the urine alcohol over that of the blood and brain. There are also considerable conflicting data in the literature regarding the amount of alcohol which is excreted in the urine. Furthermore, there is evidence to suggest that alcohol in pure form is not a true diuretic,[8] but that the congenerics contained in the vehicle in which the alcohol is in solution produce the diuretic action. Thus, the volatile oils in gin, the congenerics of whiskey and the lupulin in hops are thought by some investigators to be the active diuretic agents. Since there is a controversy not only as to the quantity of alcohol excreted in the urine, but also upon the question of diuresis, many figures obtained from the determination of urine alcohol might be subject to criticism and probably would not hold up in a court of law. Reluctance on the part of some judges to accept evidence which might cause an individual to incriminate himself unwittingly, holds true for this test as well as for the other chemical tests for intoxication.

SPUTUM

According to Abels,[9] the alcoholic content of saliva corresponds with the blood alcohol concentration within 3 per cent. It has also been observed that the rate of increase in the content of alcohol in the saliva in some cases greatly exceeds the rate of increase in the blood. Furthermore, saliva is known to contain varying quantities of oxidizable substances which in some instances may equal as much as 12 mg. of alcohol. In addition to these variables, the same criticisms may be lodged against the saliva tests as were mentioned for the urine and breath tests.

BLOOD

Next to the spinal fluid, the blood test undoubtedly comes closer in scientific accuracy than any of those just discussed, and yet the blood alcohol content as proof of degree of clinical intoxication may also be subject to serious objections. It is the opinion of Bickel,[10] the Berlin physiologist, that individual sensitivity to

alcohol must be viewed in the same light as sensitivity to other agents such as tobacco or coffee. Therefore, the determination of the quantity of alcohol in the blood as a test for intoxication cannot alone be regarded as a satisfactory criterion of drunkenness.

Holcomb,[11] of the Northwest Traffic Safety Institute, states "that through urinalysis the alcohol in the blood and thus in the brain can readily and with fair accuracy be determined," but he goes on to state that it is "the alcohol in the brain which affects the person" and it is just this point that brings up a serious question as to the efficacy of blood tests.

Vahlmering[12] was among the first investigators to demonstrate that although alcohol is about equally distributed to the visceral organs within the first hour following ingestion, the brain absorbs it more slowly, but as time goes on the brain content finally exceeds that of other organs. Moreover, he has likewise shown that not all of the alcohol ingested is destroyed or excreted for a long time.

Pringsheim[13] observed that animals with an acquired tolerance to alcohol could oxidize a given quantity of alcohol 33 per cent faster than normal animals. Furthermore, he stated that non-habituated animals reach a 66 per cent higher blood alcohol level than those animals which had become habituated. Pringsheim observed further that in the habituated animals the liver, heart and brain all burned alcohol, while in the non-habituated the liver alone seemed to be the organ which took over the major task of oxidation. He likewise observed that the visceral organs contained more alcohol than the blood in both habituated and non-habituated animals. However, "the ratio was much smaller in the alcoholic animals because of more intense oxidation."[14] In the human, Schweisheimer[15] found similar figures to be true for both teetotalers and heavy drinkers following the ingestion of alcohol, and according to Gettler,[14]

> "The results showed that the maximum alcoholic content is higher in normal persons, that it reaches this maximum in from 1½ to 2 hours, remaining at this level for five hours, and then gradually diminishes while in chronic users of alcohol it reaches its maximum more quickly, remains at this level for two hours, then subsides much more quickly."

He also states that nonusers rid themselves of all alcohol in 7½ hours, while heavy drinkers destroy it in about one-half this time. Similar figures have been given by other investigators. Schweisheimer concludes that tolerance is due to decreased maximum alcohol zone, which depends on more rapid oxidation. All of these points would seem to demonstrate that tolerance depends on the ability of the cells to oxidize alcohol rapidly. Certain figures have been obtained which tend to show that for a given degree of drunkenness there is a higher alcohol concentration in the blood of chronic drinkers than in that of non-drinkers. Thus, the initial clinical manifestations of intoxication in the average non-user are said to become noticeable at the blood alcohol level of 0.15 per cent, while in the habitual user they may not become manifest before an alcohol level of 0.2 to 0.25 per cent is reached. Even these higher levels may not give the true picture. I will quote the figures given in a recent study wherein certain case histories were cited. This investigator used the blood test for determining clinical intoxication. His figures ranged from 0.15 to 0.43 per cent. One of his subjects tested was alleged to have been an intoxicated driver who was said to have talked in a confused fashion and staggered slightly. His blood alcohol concentration was 0.43 per cent. According to all the rules relative to intoxication and blood concentration, this man should have been dead drunk, yet a jury reviewing the evidence acquitted him. Another man showed a slight retardation in buttoning his clothes and his attitude was slightly antagonistic to questioning; he had an alcoholic breath, swayed slightly in the Rhomberg test, the finger to nose test was done quickly and accurately. He walked too fast and deviated from a straight line several times. The blood alcohol level was 0.3 per cent. Again, according to the usual figures given for intoxication, this man should have been thoroughly incapacitated, yet the clinical tests were not absolutely conclusive, while the blood test branded him as totally incompetent.

From the foregoing statements it seems that even the blood test has drawbacks, as have the other tests mentioned. The blood tests merely prove that a subject's disturbed faculties may be due to the ingestion of alcohol and most juries would never accept the test alone without much more confirmatory evidence.

SPINAL FLUID, BRAIN

Now, at the outset it was stated that in my opinion there was one correct answer to the question of determining when a person is clinically and legally drunk. I have attempted to

eliminate the less satisfactory ones and have now come to the spinal fluid-brain ratio test, which I believe is the only correct one.

Gettler and Tiber[14] examined 6,000 human brains for alcohol and made up a set of tables to show the relationship between the alcoholic content of the brain and the degree of intoxication. Among the cases investigated they had "total abstainers, occasional, mild and habitual drinkers." These workers showed quite convincingly that the effects produced on all persons, no matter what the previous alcoholic habits, were in direct proportion to the alcoholic content of the brain. They likewise showed that the amount of alcohol consumed affected different people to different degrees and that the power to oxidize alcohol rapidly was often developed to a marked degree in the habitual drinker, since he destroyed it more rapidly and hence it did not accumulate in the brain. They found, however, that when alcohol once reached the brain the effect was the same on both novice and seasoned drinker.

Gettler and Tiber, as previously mentioned, demonstrated that a quantitative estimation of the alcoholic content of the brain could be relied upon invariably to indicate the degree of clinical intoxication. In these 6,000 brains which were subjected to chemical analysis, they found that in the normal brain the alcohol content was less than 0.0025 per cent. In those subjects in which a record of alcoholic indulgence was obtained, no physiologic effect from the alcoholic indulgence was noted when the alcohol content in the brain was below 0.1 per cent. When the brain content ranged between 0.1 and 0.25 per cent, some physiologic disturbance was often observed, such as increased aggressiveness and more or less loss of sense of care, yet in none of these cases was there any disturbance of equilibrium, which is the usual clinical index of intoxication. In the individuals examined where the brain content was above 0.25 per cent and from thence on up to 0.4 per cent and still higher to 0.6 per cent, definite disturbances of equilibrium were observed. They concluded from a study of this enormous series of brains that "the degree to which any person is affected does not depend on the quantity of alcohol consumed, but on the amount of alcohol present in the brain at the time."

A later study by Gettler and Freireich[16] not only confirms this earlier study, but also shows that there is a consistent ratio between the spinal fluid alcohol content and the brain alcohol content. These authors analyzed the spinal fluid, the blood and the brain from one series of cases and then studied the alcoholic content of the spinal fluid and the blood in a series of hospital cases. As a result of these studies they showed that the alcohol content of the spinal fluid could be used as an index of intoxication because of a constant and regular ratio between the alcohol content of the brain and that of the spinal fluid. It was shown that the alcohol content of spinal fluid was always somewhat higher than that of the brain and the smaller the alcohol content of the brain the greater that of the spinal fluid-brain ratio, while conversely the larger the amount of alcohol in the brain the more nearly the spinal fluid values approached the brain values. In studying both intoxicated and non-intoxicated individuals it was shown that the spinal fluid-brain ratio of intoxicated subjects was below 1.4 and ranged between 1.4 and 1.1 per cent, while the spinal fluid-brain ratio in subjects who had ingested some alcohol, but were not intoxicated was above 1.4 and might run as high as 3.1. Furthermore, all cases which showed 0.265 per cent or more of alcohol in the spinal fluid were clinically intoxicated. This latter figure corroborates the previous observations of Gettler and Tiber, which demonstrated that subjects with an alcoholic content of the brain of over 0.25 per cent were clinically intoxicated.

Of added interest were their findings in regard to the blood alcohol concentration as an index of intoxication. In this series of necropsied patients they found that the alcoholic content of the blood varied greatly when compared to the brain alcohol content and that it might be either higher or lower. Moreover, they showed that the blood-brain ratio might vary anywhere between 0.66 and 0.55 per cent, thus demonstrating the complete lack of uniformity in the blood-brain ratio as compared with the striking and constant uniformity of the spinal fluid-brain ratio with reference to clinical intoxication.

This work seems to have demonstrated rather conclusively that blood alcohol determinations are not very reliable. It is also interesting in this respect that the figures which are usually accepted as an index of intoxication, based on a blood alcohol percentage of 0.15, should not be used as evidence in determining the degree of intoxication, since Gettler and Tiber found that some cases in which the alcoholic content of the brain was between 0.2 and 0.25 per cent showed

no disturbance of equilibrium and that persons with an alcoholic content below 0.2 per cent were not intoxicated.

CONCLUSIONS

In conclusion, I should like to emphasize the following points:

(1) The diagnosis of drunkenness and particularly the degree of intoxication is subject to many pitfalls both medical and legal, and there is even much disagreement of opinion as to what constitutes alcoholic intoxication.

(2) There are many clinical variables which must be carefully considered before a diagnosis of drunkenness should be rendered. There are also many psychological variables which must be given consideration.

(3) It seems from the large volume of investigative work that none of the standard tests of analyzing body fluids except chemical analysis of the spinal fluid can be used with uniform accuracy to determine the brain alcohol content. Since the spinal fluid-brain ratio is constant, the spinal fluid appears to be uniformly applicable for determining the brain content of alcohol. This latter procedure certainly should require the consent of the accused and it cannot be carried out without a certain degree of danger, hence the spinal fluid test will probably never be brought into general use except in institutionalized cases.

BIBLIOGRAPHY

1. Hall, W. W.: Drunkenness: Naval Medicolegal Aspects of the Diagnosis. U. S. Nav. Med. Bull., **34**:149 (April) 1936.
2. Surtees, R. S.: Handly Cross, or Mr. Jarrock's Hunt, **2**:700. Eyre & Spottiswode and Charles Scribner's Sons, London and New York 1929.
3. Dickson, E.: The Medicolegal Aspects of Drunkenness. I. Med.-Leg. & Criminol. Rev., **3**:274 (Oct.) 1935.
4. Personal communication.
5. Ebel: Die Wissenschaftlichen Grundlagen der Beurteilung von Blutalkoholbefunden, page 93, quoted by Quieries and Minor Notes. Effect of Shock on Drunkenness. J.A.M.A., **112**:464 (Feb. 4) 1939.
6. Harger, R. N.; Lamb, E. B.; and Hulpieu, H. R.: A Rapid Chemical Test for Intoxication Implying Breath. J.A.M.A., **110**:779 (March 12) 1938.
7. Carter, G.: Tests for Drunkenness in Relation to Motor Accidents. Jour. Med. Soc. N. J., **35**:537-541 (Sept.) 1938.
8. Mendel and Hilditch, quoted by Wallace in Haven Emerson's "Alcohol and Man," p. 53. New York: The Macmillan Co., 1933.
9. Abels, J. C., quoted by Selesnick, S.: Alcoholic Intoxication. J.A.M.A., **110**:775-778 (March 12) 1938.
10. Bickel: Berlin Letter. J.A.M.A., **106**:2171 (June) 1936.
11. Holcomb, R. L.: Alcohol in Relation to Traffic Accidents. J.A.M.A., **111**:1076 (Sept. 17) 1938.
12. Vahlmering, Jr., quoted by Gettler and Tiber. Zentralbl. biochem. Biophys., **14**:520, 1912 (See Ref. 14).
13. Pringsheim, quoted by Gettler and Tiber. Biochem. Ztschr., **12**:143, 1908 (See Ref. 14).
14. Gettler, A. O.; and Tiber, Arthur: The Alcoholic Content of the Human Brain: Its Relation to Intoxication. Arch. Path. **3**:218-226 (Feb.) 1927.
15. Schweisheimer, quoted by Gettler and Tiber. Deutsche Arch. f. klin. Med., **109**:271, 1912 (See Ref. 14).
16. Gettler A. O.; and Freireich, A. W.: Determination of Alcoholic Intoxication During Life by Spinal Fluid Analysis. Jour. Biol. Chem., **92**:199-209, 1931.

DISCUSSION (*Abstract*)

Symposium on Legal Medicine, papers of Dr. Roger D. Baker, Dr. George S. Graham, and Dr. Ferdinand C. Helwig. Paper of Dr. Baker was published in the April issue, page 411; paper of Dr. Graham in May, page 546.

Dr. Owen S. Gibbs, Memphis, Tenn.—There is at the present moment in this country a developing interest, spreading still too slowly for some of us, in medicolegal and toxicologic matters.

Since 1921, we have nearly 2,000 case records in the John Gaston Hospital of poisoning alone. This does not include other medicolegal injuries of great importance. Medical jurisprudence rests on a tripod. The first is pathology, the second is pharmacology, and the third is law. These three legs support the public weal. The importance of the medicolegal work is the public, and that is its raison d'etre.

All three subjects must be modified and conditioned by certain peculiarities associated with the application of this work. This requires experience and special training. Even the pathologist, who is perhaps normally more closely associated with the workings of medicolegal problems than his colleagues, may, by reason of inexperience or failure to carry the fruits of his observations and of his knowledge to the layman, which include, of course, the lawyers, be much less valuable in this field than might be expected.

In the same way some pharmacologists, especially those with deficient training, have not access to the human animal houses, meaning the hospitals, and when faced with the practical problems associated with the more potent actions of their drugs, fail rather miserably in medicolegal affairs.

Speaking with less technical knowledge but still with a fair assurance, I feel safe in saying that members of the legal profession, also not specially experienced in this type of work, may lose their cases as a consequence of their failure to appreciate and utilize scientific testimony correctly.

I agree, therefore, with the authors of these three admirable papers in which they stress the necessity of having available trained men and suitable laboratories where adequate tests and proper examinations, under the necessarily more stringent legal requirements, can be carried out. Failure to appreciate these necessary requirements has led to the development of a situation which is already becoming a ripe harvest. I refer to the medical expert. In some cases men have been permitted to qualify as expert witnesses for the particular case or, indeed, for any case, on totally inadequate grounds. Many expert witnesses give testimony in courts which is based merely on a certain knowledge of literature, without any practical experience. This may result not only in isolated injustice, but, in the creation on the one hand of dangerous legal precedents which may misguide other jurisdictions, or alternately—I think this is the lesser evil—it has thrown doubt on the testimony of all experts in the courts of law, with the consequent loss to these authorities of their respect for the guidance of science.

Personally, I can do nothing about this matter except

assist others in calling attention to its urgency. However, one feels that a distinction between ordinary professional information and real specialists' information should be carefully drawn in a court of law.

To clarify this statement, may I give one example? As a laboratory academic pharmacologist, I would unhesitatingly testify that lead tetra-ethyl is a dangerous, diabolic, and deadly poison. As a practical man, having some knowledge of the use of lead tetra-ethyl, especially that tons and tons of the stuff are distributed all over the country in the form of ethyl gas, I could testify with equal assurance that as a substance used by the general public in this form it is harmless. This example also illustrates the contrast between the flat, two-dimensional knowledge of the reader and the three-dimensional knowledge of the experienced practical man. It is this latter type of information that the courts really need, for resting on their decisions may be the fate of human liberty or even life itself, which is, incidentally, of far more academic interest to the persons involved.

In reality, the untrained "expert" may constitute a real source of danger, and this is actually aggravated by the fact that men who consistently appear in courts as experts are not infrequently, in a rather derogatory manner, referred to as "professional experts," which, cleverly conveyed to a jury, may suggest bias and prejudice. Actually, such men are, if properly trained originally and equipped with facilities for broadening their knowledge, far more valuable to the courts than the other type of "expert."

Thus we find that experience and training are necessary, first of all, to make medicolegal observations; secondly, to formulate practical and real answers to those observations; and, thirdly, to convey this information in simple, correct medicolegal language to a lay people. Clearly, the haphazard system of medicolegal work which is now existing is of questionable value and sometimes I am rather inclined to believe of even less questionable danger to the public.

If, as is clearly shown by the extent and number of medicolegal cases and problems, the public weal needs such service, it must be removed from the semi-professional status now existing.

One of the speakers has very correctly drawn attention to costs. Medicolegal examinations are necessarily costly. They are difficult, they are expensive, and they are sometimes very long-winded, indeed. But, since it is a public problem, the cost must be borne by the public. No matter in what way it comes, either from the police, the state, the FBI, or another government agency, the public still pays the bill. Before the public should be asked, or made to do so, which seems to be the modern custom in paying such bills, adequate justification for this should exist. There is, however, already adequate justification, because enormous numbers of practical problems exist, such as our example of 2,000 cases of poisoning, very few of which have been investigated from a medicolegal angle, because no facilities exist.

It is clear, therefore, that a laboratory with an adequate equipment and staff, directed by at least one man trained in this field, should be available in all states, and it should be located at a strategic point. Such a laboratory naturally demands access to a library, and it also demands access to men who are highly specialized in other fields, which one single man cannot possibly cover.

We have already had a description of a laboratory which now exists in this country, or a system, shall we say, in Maryland, which is a new step. The best system I have personally encountered was in old Vienna, where there was a government institution, and, quite automatically, every person in the university who was considered sufficiently well trained to be an expert, even perhaps in one small line, became a consultant to this central department. The Viennese system was astonishingly good. Also, I had the opportunity, fortunately, of studying in a school where medicolegal work was considered a major subject, namely, Edinburgh, Scotland.

Such a laboratory, of course, would entail a certain amount of costliness. On the other hand, I think the problems today are of such practical importance that they would justify at least one such laboratory in every state. This most beneficially would cooperate with medical schools, the police, and the courts. There are also several large industrial problems that exist in any single state. Indeed, there is hardly a state in this country that does not have its own industrial medicolegal problem, usually of a toxicologic character.

Finally, may I be permitted to emphasize that the major importance of medicolegal work depends on the needs of the public. It is required for their guidance and protection, and it must be carried out in accordance with their proper laws and constitutional rights.

The courts not infrequently are slow, and occasionally fail to arrive at a just conclusion in highly technical matters. Nevertheless, any attempt to subvert the rights of free men, or the proper court procedures, even with the "best intentions," which is so characteristically the paving of a different world, must be regarded as a treatment far more dangerous than the disease.

I personally feel that medical jurists must never permit their scientific interest to overstep the legal boundaries laid down in this country, which order remains free because these boundaries exist.

The carrying out of experimental procedures, for example, spinal puncture, on arrested persons either by fraud, by trickery, by other forms of chicanery, or by actual force, while tempting to the scientist and still more tempting to some enthusiastic prosecutor, will nevertheless lead to such weakening of the human rights and liberties as to constitute a condition far more serious than any which exists at the present time in this country.

Therefore, while I am in favor of good medicolegal work, soundly established, with adequate, trained personnel, nevertheless I would be the first to denounce any attempt to force dangerous tests or any other infringement on the human rights of his own person in the conduct of these tests. Otherwise they would eventually result in such a feeling of public hatred that the subject would be retarded from its normal growth.

Dr. Wiley D. Forbus, Durham, N. C.—I do not know of anything that is quite so frightening for the pathologist and for the doctor in general as a court. Doctors, being pathologists as well as clinicians, are inclined to avoid the courts as our European neighbors would avoid the bombs that drop from the sky. There

must be some reason for that, and of course we know there is a reason. If that is generally true, and I think it is, one perhaps has to give some explanation of his interest in a scheme of this sort.

Our own interest in medicolegal problems was stimulated by two things: first of all, a necessity for knowing something about it; and, secondly, a thing which is oftentimes condemned in pathologists, and that is a slight sense of social consciousness.

As a result of these two factors we started in our laboratories about seven or eight years ago, and in collaboration with the law school of our university, a program for the study of medicolegal problems, and it was done with the idea of trying, if possible, to see if we could work out a scheme of things which would bring the lawyers and the doctors just a little bit closer together in dealing with a problem which is obviously common to them both.

During the past seven or eight years, then, we have carried out a series of studies of real cases. Of course, somebody had to get those cases, and it happened that that fell to my lot in some instances and to others in other instances, but my own cases are the ones which taught me most, of course.

I have learned from practical experience with the actual cases and also with the practical experiences of trying these cases within a controllable body, that is, a body of medical students and a body of law students with medical advisers and legal advisers all interested in the problem of education, that there is such a tremendous gap between the point of view of the lawyer and the doctor that unless something can be done about that from a political point of view, we shall always be faced with the almost insurmountable difficulty of making available what we know.

So my remarks are directed especially toward the matter of bringing before the court, or before the body, whatever it is, the data which we know how to get. It is perfectly obvious from the papers that have been given here this morning that we do know how to find medicolegal facts; that there is really no problem that we cannot offer a pretty satisfactory solution for if we are given the opportunity. We may get the facts, we may have the case prepared in a way which to the medical man will be absolutely satisfactory and safe and sound, but we shall not be able to get those facts before the court.

This is well known to all of you, and I am sure I am boring some of you by even mentioning it, but I want to tell you just very briefly of two instances where inability to get before the court facts of this sort seemed to me to illustrate the tremendous problem we have.

Rather recently I had occasion to be drawn into the Federal District Court of North Carolina on a case which involved the simple problem of suicide, or death from other causes. I will not go into the details of that. I will ask you to accept this, that the problem was a perfectly simple one to determine. It involved no trick procedures. Anyone who was the least familiar with investigations of that sort could arrive at a conclusion without any difficulty as to whether the gun was at a certain place or not. Perhaps I ought not to tell this, because it admits it is a failure, but it took six hours for the attorneys on the opposing side to get before this very intelligent judge and what I thought was a very intelligent jury facts which neither the judge nor the jury could interpret. So the outcome of all that work was that there was nothing accomplished. That was in what I regard as one of the highest types of courts we have. It certainly was the most dignified procedure and the most intelligent court procedure I had had any experience with.

The other experience involved a court of what I think we might call low water, and I think the lawyers would say it was not a court at all, that is, a compensation commission. As you well know, compensation commissions are really classified by lawyers as administrative bodies rather than as courts, and they have legal procedures that are quite different from the courts.

The case that came before that commission was one which involved a diagnosis. A surgeon had operated upon a patient and made a diagnosis which he, himself, admitted to be only a preliminary diagnosis, and which he admitted to be of great uncertainty. The interested parties brought the case before this commission for the purpose of obtaining permission to investigate the case to find out what really was the matter. It involved the performance of an autopsy.

The commissioner heard the case. He ruled that he would not permit an autopsy. He would not permit an autopsy because a diagnosis had been made and that was all that was necessary. For about a whole day an attempt was made by the interested party to bring before that court certain facts and opinions, and so on, which would convince him that a diagnosis had not been made, but he felt sure that since a diagnosis had been made he did not wish to go against the wishes of the family in that case.

So the point was this: the judge, or the commissioner, assumed the responsibility of making a medical diagnosis which, of course, was absolutely impossible for him to do even had he had all the facts, and in that case nobody had any facts.

Those are two extremes, but they do illustrate as best I can what I mean when I say it is extremely difficult to get before a court the essential facts upon which it can act.

It is all well to criticize; it is all well to find fault, but what is the solution to such a problem? I have given some thought to it. It is an interesting thing, and it seems to me one thing will solve the problem, and that is to set up another administrative body whose duties it will be to bring into court facts and opinions, to deliver over to the court, not to the jury, not to the lawyers, and so on, facts and then have those facts acted upon in so far as they influence legal decisions.

What kind of a commission shall it be, what kind of an administrative body? First of all, it should be one which is appointed by the court, not by contending parties. Secondly, it should be made up of, I think, fundamentally three types of people; it should be made up of a surgeon, an internist, and a pathologist. They may be supplemented by what other specialists, you might say, would be required to settle a given point.

But lay the medical problem before that medical commission, have it render a decision as best it can, have it render an opinion, and have the court act on that opinion.

I am perfectly sure the lawyers would tear such a thing as that all to pieces, and even, I think, Dr. Gibbs might object to that because it might interfere with some of the rights we have in courts, but I see no way of getting around the tremendous difficulties which the rules of evidence make and which court procedures make than by such a measure as that.

Dr. J. A. McIntosh, Memphis, Tenn.—I was impressed with the indefinite presentation of exact information. It is impossible to tell when a man is drunk, almost, because of the many conditions that exist at the time he takes the alcohol. For instance, if he attends a banquet and partakes of butter and gravy, the alcohol slowly enters the circulation. Many persons who attend public banquets and drink excessively have learned the trick of using butter to inhibit the rapid absorption of alcohol.

Then, too, I recall an experience I had in this city of a boyhood friend who was arrested on the streets and jailed for driving crooked. His wife called me and asked me to come to the city hall and help get him out of jail, that he did not drink. I found my friend in the cell, somewhat confused. He told me he did not drink, but he had been taking atropine. The only relationship I can think of between atropine and ethyl alcohol would be a similar action on the vasomotor center. It affected this man's driving ability. The police accepted that as evidence of his being drunk.

Frequently I am called upon to act as a witness, just as Dr. Gibbs has acted. I think common sense and honesty perhaps stand the doctor in better stead than profundity. Conclusions from common, everyday experience help him more than technical knowledge.

Medicolegal matters seem to me to be growing. The government is in the social security business in a big way and, from the trend of things, it seems that soon insurance will be in the hands of the government even more extensively than at present. Most of the medicolegal autopsies that I have originate through insurance companies. They will not pay out money if they can help it, and perhaps it is all right to be that way. They want facts, and they pay liberally for those facts.

The government will eventually become interested in determining exact causes, and having facts such as Dr. Forbus declares useful. It is time for the schools to train students for this service. I hope our local school will take serious consideration of training young students in medicolegal necropsy procedures and testifying convincingly before juries.

Dr. Helwig (closing).—I should like to correct a possible misunderstanding. I certainly do not mean to imply that I advocate the wholesale employment of spinal puncture as a diagnostic aid in drunkenness and I think it should be emphasized that this would be a very dangerous procedure. Moreover, I should like to correct any possible misconception that I think we do not have an extremely efficient police department in my home town, since I am convinced it is the best we have had in thirteen years.

INDICATIONS FOR AND RESULTS OF SPLENECTOMY*

By H. Dale Collins, M.D.
Oklahoma City, Oklahoma

The case records in two of our larger hospitals show that thirty-one splenectomies have been performed in these two institutions during the past fifteen years. These cases have been reviewed and their results will be reported in this paper.

The indications for splenectomy offer a rather intriguing problem, since the spleen is one of those enigmatic organs whose functions are only partially understood. It will be well to review briefly some of the known functions of the spleen, in order to understand the indications for splenectomy.

The spleen acts as a reservoir or storage house for the general circulation and has the power of contractility. It is somewhat of a governor of the portal circulation of which it is an integral part. The spleen is a part of that extensive and inadequately understood reticulo-endothelial system which has as some of its functions blood formation, blood destruction, filtration and phagocytosis of bacteria, toxins and foreign material. The spleen plays a part in the metabolism of fats. It has the power of producing lymphocytes. Most physiologists believe that the spleen is largely responsible for the presence of platelets in the circulation; however, the mechanism is little understood.

The large majority of cases in which splenectomy is indicated falls into one of the following headings: congenital hemolytic jaundice, primary thrombocytopenic purpura, so-called Banti's disease or splenic anemia, and injuries of the spleen.

The diagnosis of splenic disease should be approached with due caution. Improper diagnosis and therefore unwarranted splenectomy have been responsible for many fatal results. Fortunately we have been greatly aided in the past few years by the notable efforts of the hematologist, physiologist and the pathologist. Their findings have been an immeasurable aid in the proper diagnosis of splenic disease. Every effort should be made to arrive at the proper diagnosis. Certainly a complete blood study

*Read in Section on Surgery, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

should be made. Careful study of pathologic findings at operation will be productive of better results. This will be discussed more fully later under Banti's disease. Haden[1] suggests a diagnostic aid which may be used to advantage in certain cases. He says that irradiation may be used to exclude certain diseases of the spleen. If irradiation lessens the size of the spleen, splenectomy is not advisable. This aid will exclude operation in cases of leukemia and Hodgkin's. Another large group of cases which produce splenomegaly can be excluded generally, as Cohn[2] suggests that splenomegaly associated with acute febrile reactions is rarely benefited by splenectomy. These two mentioned generalizations are worth remembering when we consider splenectomy.

Let us now consider each of the major causes for splenectomy.

Hemolytic jaundice is a chronic or recurring type of anemia, associated with an icterus which increases during crises of hemolysis. The spleen is enlarged, urobilin increases in the urine and the stools, the fragility of the red blood cells is increased, and the red cells are smaller in diameter, but increased in thickness. These cells are known as spherocytes. The spleen apparently filters out these red blood cells and this produces the anemia and the jaundice. Hemolytic jaundice is sometimes divided into a congenital and an acquired type. There is considerable doubt that an acquired type exists, although many years may elapse before the signs and symptoms of the disease present themselves.

If the diagnosis is properly made one may expect a complete and permanent cure in these cases. In our series of cases we have operated upon five with congenital hemolytic jaundice with one death. The ages varied from 7 months to 44 years at the time of operation. We prefer not to operate upon these cases during an acute crisis, but rather to wait for a quiescent stage of the disease. Eliason[3] believes that occasionally one must operate during an acute exacerbation to prevent a fatality. In this particular group of cases we had one of more than usual interest, a case of hemolytic jaundice associated with infantilism in a male, aged 11 years. Splenectomy was performed; he made a prompt recovery from the splenectomy, and he has also made excellent strides toward normal skeletal and glandular development. This case has been reported in detail by Langston and Turner.[4]

In institutions where a large number of these cases are operated upon the results have been striking. The Mayo Clinic reports 118 cases with a mortality of 3.4 per cent.

Caution is necessary in the diagnosis of hemolytic jaundice. There are cases which present the signs and symptoms of this disease which do not present the characteristic spherocytic red cells. We had two such cases and in both instances a malignant tumor of the spleen was found. These two cases recovered from the operation, but died later of their malignant disease.

Purpura hemorrhagica or thrombocytopenic purpura is a disease characterized by purpuric spots in the skin, hemorrhage from the mucous membranes and a tendency to bleed excessively from cuts or traumatized tissue. There are two principal types of this disease, one without demonstrable cause (idiopathic thrombopenic purpura) and a secondary type which may be due to sepsis, toxins, drug poisoning, Gaucher's diseases, pernicious anemia, leukemia or aplastic anemia. True idiopathic purpura is much less frequent than the secondary type of the disease. However, splenectomy is warranted chiefly in the idiopathic group. The characteristics of the blood are most important in the diagnosis of this condition. There is a marked diminution or almost an absence of the blood platelets or thrombocytes; and a prolonged bleeding time associated with a normal clotting time, but poor clot retractility. The tourniquet test is usually positive.

Again the correctness of the diagnosis is most important. We have seen a large number of cases of purpura, but only five of them have been diagnosed as primary or idiopathic. Five cases have been operated upon with three recoveries. Two of these were not true idiopathic purpuras. One patient died soon after with a septicemia; the other succumbed a few weeks later from an infectious process which was evident at operation. Two of the recoveries have been complete, while the third, after a period of quiescence for five years, has now again appeared with evidence of the former purpuric tendencies.

One of these cases stands out very clearly.

A white boy, aged 9, had received a large number of transfusions before his entrance into the hospital, and he received a considerable number more while being prepared in the hospital. It was absolutely impossible for us to control his acute purpuric tendency and operation was decided upon. At operation there was

considerable bleeding from all cut surfaces in the abdominal wound. Control of hemorrhage was for the most part futile. Fortunately the spleen was not greatly enlarged and there was a long splenic pedicle which allowed the spleen to be brought into the wound easily. The pedicle was clamped and within a brief time, one or two minutes at the most, the bleeding in the abdominal wound ceased and never recurred. This phenomenon would suggest the possibility that idiopathic purpura is caused chiefly by an abnormality solely within the spleen.

Yet as more cases are being operated upon and as follow-up histories develop, we note that a certain number have recurrences of their purpuric tendencies. Some investigators believe this is due to the development of accessory spleens and other causes are suggested.

We now approach the frequently discussed Banti's disease. I think we can all agree that some additional facts have been presented relative to the symptom-complex, since Banti[5] first described it. Banti's criteria for diagnosis were: an enlargement of the spleen associated with anemia of varying severity; leukopenia; hematemesis; and sometimes ascites. He described a definite lesion of the spleen and believed that the spleen was largely responsible for the other pathologic findings. Apparently Banti described a syndrome which has included a variable pathology and in which he believed that cirrhosis was an inevitable consequence.

A considerable amount of information has been acquired that should be of value in describing conditions similar to Banti's disease. Experimental work reveals that any increase in pressure in the portal system produces a resultant venous congestion. The spleen enlarges in size and if the congestion is maintained, fibrosis develops. Such a fibrosis develops in the liver in cirrhosis of the liver and thrombophlebitis of the portal splenic veins. Therefore it is probable that portal congestion from one cause or another is largely responsible for the splenomegaly of Banti's syndrome. One cannot help being struck by the similarity of the vascular changes in Banti's disease regardless of the causative factors, whether obstruction, hypertension or another condition. The blood vessels are always greatly enlarged, the circulation is more than adequate and this produces one of the severest hazards in this operation. Rousselot[6] was able to demonstrate in certain cases a definite increase of the portal pressure. However, it must be assumed that at operation a very detailed examination of the portal bed is not always within the realm of possibility and perhaps an obstructive factor is present more often than is demonstrated. Attention to the possible etiology of Banti's syndrome may be of considerable help to us in the management of cases which are now diagnosed as Banti's disease or splenic anemia. Certain it is that we need some help in the management of these cases because the results have not been too promising. Rousselot, in his excellent treatise on Banti's disease, has presented a very complete classification of pathologic conditions that produce this syndrome. He emphasizes the necessity for differentiating the etiologic factors. Among thirty-one cases he found fifteen with no evidence of an obstructive mechanism, and these cases showed no evidence of cirrhosis. In the remaining sixteen cases he noted evidence of an obstructive factor and grouped these cases upon the following pathologic basis: 9 cases of Laennec's cirrhosis (hobnail liver); 2 cases of cirrhosis, unclassified; 2 cases of schistosomiasis; 2 cases of thrombosis of the splenic vein, and 1 case of cavernomatous transformation of the portal vein. The fifteen cases of undemonstrable portal obstruction are most important because he chooses to classify these under the designation, portal hypertension, as suggested by McMichael.[7]

In the series of cases reported from the Spleen Clinic at the Presbyterian Hospital in New York, hematemesis was found to be a bad prognostic sign. These cases had a higher mortality rate and a lesser number were improved by operation.

Hanrahan[8] believes that a more careful inspection at the time of operation will assist in making decisions that will be beneficial from the standpoint of prognosis following splenectomy. He believes that if, at operation, one finds an atrophic cirrhosis of any appreciable degree splenectomy is rarely beneficial. If the lesion is a thrombosis or stenosis of the portal system, the basis for splenectomy must be that the prognosis is bad at best and there may be some improvement by splenectomy. In those cases without demonstrable obstruction the results are much more encouraging than in the other cases which show obstruction.

We believe in the consideration of our experience with splenectomy in Banti's disease that much more attention must be given to the cause of the splenomegaly in any given case. Experience has shown that certain cases of Banti's syndrome do not warrant operation. It is absolutely impossible to know definitely before operation, in certain instances, just what the

pathologic condition may be and in many cases an exploratory procedure will definitely determine the advisability of splenectomy.

We have had fifteen cases of Banti's disease with five operative deaths. Unfortunately our records did not reveal sufficient information to allow us to describe the pathologic conditions coexisting with the enlarged spleen and it is impossible for us to group our cases according to the pathologic basis suggested by Rousselot. However, I am sufficiently impressed with these reports to believe that they warrant very definite consideration. Certainly our own operative results have not been sufficiently good for us to be satisfied with the operative management of cases diagnosed Banti's disease. Of the ten patients who recovered from the operation, six have returned with hematemesis, and three of this number have subsequently died.

Goldhamer[9] reports an operative mortality of 30 per cent and the follow-up on his cases reveals that those which were not operated upon probably did as well as those that were operated upon. Our experience has been somewhat similar to this report; however, we have had at least three cases that appear completely well following splenectomy.

The last group demanding splenectomy in our series contains those classified as having a ruptured spleen. Ordinarily, rupture of the spleen is associated with severe trauma to the abdomen or lower left chest, but one case in this group is an exception.

This particular case occurred in a white man aged 27. He had had malaria for a considerable time prior to rupture of the spleen. Rupture of the spleen occurred as he stooped to pick an object from the floor and in doing so he twisted his body and suddenly suffered severe agonizing, left upper abdominal pain. His symptoms were those attending a ruptured viscus. At operation he was found to have an intraperitoneal hemorrhage from a ruptured spleen. The spleen was considerably enlarged. The pathologist's report was infectious splenitis.

This is a rather rare condition, but it must be borne in mind in certain cases of splenomegaly. This man recovered from the operative procedure and was well six years following the operation. We have operated upon four cases of ruptured spleen, with recovery in each instance. There have been other cases with ruptured spleen with other coexisting serious injuries in which the condition of the patient never warranted splenectomy. We feel that splenectomy is indicated in all cases showing evidence of rupture as soon as the condition of the patient warrants surgery.

CONCLUSION

(1) We believe that the majority of cases demanding surgical removal of the spleen fall into one of four groups: thrombocytopenic purpura, congenital hemolytic jaundice, Banti's disease, and injuries to the spleen.

(2) Good results may be expected in the treatment of congenital hemolytic jaundice with splenectomy.

(3) The diagnosis of thrombocytopenic purpura must be made with great care and every effort must be made to exclude other confusing types of purpura if good results are forthcoming.

(4) More attention must be given to the coexisting pathologic conditions in Banti's disease.

(5) Traumatic rupture of the spleen is followed by excellent operative results in the absence of other serious lesions.

BIBLIOGRAPHY

1. Haden, R. L.; and Dinsmore, R. S.: Indications for Splenectomy. Surgical Clinics of North America (Oct.) 1937.
2. Cohn, I.: The Differential Diagnosis and Surgical Indications of Splenomegaly. Sou. Med. Jour., **31**:486 (May) 1938.
3. Eliason, E. L.; and Johnson, J.: Surgery, **2**:— (Dec.) 1937, pp. 823-834.
4. Langston, W.: Hemolytic Icterus with Infantilism. Sou. Med. Jour., **28**:316 (April) 1935.
   Turner, H.: Anterior-Pituitary Dwarfism: Further Report of Cases Treated with the Growth Hormone. Sou. Med. Jour., **28**:309 (April) 1935.
5. Banti, Quido: Splenomegalie mit Lebercirrhose. Beitz. Z. path. Anat., **24**:21, 1898.
6. Rousselot, L. M.: The Role of Congestion in So-called Banti's Syndrome. J.A.M.A., **107**:1788-1793 (Nov. 28) 1936.
7. McMichael, J.: The Portal Circulation. Jour. Physiol., **75**:241 (June) 1932.
8. Hanrahan, E. M., Jr.; and Vincent, Beth: Surgery of the Spleen. Lewis' Practice of Surgery, —:—. W. F. Prior Co.
9. Goldhamer, S. M.: Splenectomy in Hematopoietic Disorders. Univ. Hosp. Bull., **2**:20 (April) 1936.

DISCUSSION (*Abstract*)

Dr. Giles A. Coors, Memphis, Tenn.—It is quite obvious to all of us that the policy of removing spleens indiscriminately, which was popular up to about fifteen years ago, has gradually given way to more accurate diagnosis, particularly by the pathologist and hematologist. Now we have narrowed down the indications for splenectomy to practically the same conditions that Dr. Collins mentioned in this paper.

We should be guarded in promising patients suffering from Banti's syndrome much relief, especially after there has occurred hemorrhage from the gastric mucous membrane, since only about one-fourth who show gastric hemorrhage before operation are free from it following splenectomy.

The remarkable and permanent good results following splenectomy for congenital hemolytic jaundice with an enlarged spleen stand out spectacularly. True purpura is next in line of expectancy of good results, but they are not quite so constant following splenectomy as in cases of hemolytic jaundice.

Here in the South we have a provincial problem in sickle cell anemia which is probably a congenital condition affecting the erythrocytes, seen prevalently in the negro race. In this type of anemia, if splenectomy is performed early, fairly good and constant results are to be expected. However, the results in this type of anemia are not so reliable or predictable as those in familial jaundice. In the second more or less localized affection, namely, the tremendously enlarged malarial spleen which is at times enormous and extremely friable and which at the same time makes the complete eradication of malarial plasmodia practically impossible, we feel occasionally justified in removing spleens which are radioresistant and extremely vulnerable to trauma.

In several cases of traumatic rupture of the spleen I have observed that the capsule is not ruptured, the symptoms of shock are greatly delayed and the subcapsular hemorrhage, which may later rupture, has been strongly evidenced and suggested by quite high leukocyte counts, in the high twenties and up into the thirty thousands. Because the spleen is obviously not an absolutely essential organ to bodily well being, I believe it is not wise to attempt to temporize and treat conservatively ruptured spleens, but on account of the strong likelihood of blood-borne late infection producing splenic abscess in ruptured spleens that have been treated conservatively, to practice splenectomy as early as the patient can stand surgery.

I have had the experience of operating upon a boy about 15 years of age who ruptured his spleen while falling on the handle bars of his bicycle. After splenectomy, he completely recovered and grew up to be a high school football celebrity and later to be picked as an all-Southern halfback, which is pretty good evidence that a spleen is not necessary to robust health.

JOHN GASTON HOSPITAL

Last Ten Years

16 Cases Splenectomy

6 Ruptures
3 Wounds (stabs, gunshot)
3 Splenic anemia (sickle cell)
2 Malarial splenomegaly
1 Sclerosis of liver, splenomegaly (probably Banti's disease)
1 Hemolytic jaundice (hereditary)

BAPTIST HOSPITAL

Last Fifteen Years

29 Cases Splenectomy
6 Deaths

2 Banti's disease (no deaths)
2 Thrombocytopenic purpura (no deaths)
5 Hemolytic jaundices (no deaths)
8 Ruptures (4 deaths)
1 Myeloid leukemia (1 death)
8 Malarial splenomegaly (1 death)
1 Melanosarcoma, metastatic, of spleen (operative recovery)
1 Splenitis with abscess formation (no death)
1 Splenitis, chronic interstitial

THE ROENTGENOLOGIC BONE MANIFESTATIONS IN CERTAIN GENERALIZED DISEASES OF INFANTS AND CHILDREN*

By W. D. ANDERSON, M.D.
and
JAMES G. HUGHES, M.D.
Memphis, Tennessee

In pediatric practice many conditions produce certain changes in the long bones which can be demonstrated by x-ray studies and may enable one to arrive at a correct diagnosis of the disease. In addition, studies of the long bones may frequently bring to light unsuspected conditions in their early stages, thereby insuring treatment in some cases before permanent damage has taken place. For these reasons, we believe that a description of the most important of these conditions with their x-ray findings will be helpful to those who wish to make this examination a more frequent procedure.

We have classified the material in this presentation under five main groups:

(1) CONGENITAL ANOMALIES

(1) *Albers-Schönberg Disease* (*Osteopetrosis or Marble Bones*).—This extremely rare condition is characterized by increased density, thickness and brittleness of the bones, associated with a tendency to pathologic fractures. In addition to pathologic fractures, encroachment on foramina of the skull occurs so that the patient may be blind from optic atrophy, or deaf, or suffer from nasal obstruction and interference with drainage of paranasal sinuses. Enlargement of the ends of long bones, scoliosis, pigeon breast, and coxa vara may be noted. Death occurs from intercurrent infection or from aplastic anemia due to bony encroachment on the marrow.

On roentgen examination, all or most of the bones present a dense white, chalky or sclerotic appearance with loss of normal trabecular markings. The increase in the size of the cortex gradually causes encroachment on the medullary canal. There may be a peculiar fluting of the ends of the femurs. The condition usually manifests

*Read in General Clinical Session, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

itself first in the ends of the long bones and may eventually involve the entire skelton.

(2) *Osteogenesis Imperfecta* (*Fragilitas Ossium*).—Osteogenesis imperfecta is a rare congenital abnormality of bone, due chiefly to defective membranous ossification and characterized by slender, fragile bones which fracture easily. Defective ossification of the skull bones occurs, leading to deformities of the skull. Repeated, usually painless, fractures of long bones result in healing with deformity, producing shortening and bending of the extremities. In those cases definitely of an hereditary nature the defect is transmitted as a dominant mendelian factor. Sporadic cases without hereditary background occur. In some cases fractures are delayed until after the first year, or later in childhood, or even in adult life. In some instances, blue sclerae, relaxation of ligaments and deafness due to otosclerosis accompany the bony defect. Three general types are usually described.

Roentgen examination in the congenital type shows the bones markedly deficient in calcium and therefore radiolucent. Most long bones show excessive curvature and malposition. Due to the calcium deficiency, frequent fractures occur which heal with excessive callus and marked deformity. The skull bones are very thin and may show only occasional placques of calcium. Most of the cases of this type are either born dead or die within a few months after birth.

Infantile and late types probably represent different stages of the same type with only a difference in the date of appearance of symptoms. The skull bones are very thin. The frontal bosses are bulging and the head is large. The unbroken long bones are of normal length, but very slender and show excessive curvature. This bowing is usually laterally in the femora and medially in the tibiae and fibulae. Deformities are encountered throughout the skeleton due to multiple fractures. As the curvature develops, new bone is laid down along the concave surface, causing the medullary canal to migrate toward the convex surface.

(3) *Chondrodystrophia Foetalis* (*Achondroplasia*).—Chondrodystrophia foetalis is a congenital bony anomaly in which endochondral ossification is defective. As a rule the child dies *in utero* at about the eighth month. Those who are born alive may soon die, but in other instances survival to old age may occur. The patient has a characteristic appearance: dwarfism in which the arms and legs particularly are shortened, large head, pug nose, normal trunk as a rule, lumbar lordosis, protuberant abdomen, and pudgy trident-shaped hands. There is frequently sexual precocity. Mentality is normal. The condition is apparently due to defective germ plasm.

A somewhat similar condition known as Morquio's disease will not be discussed here.

The roentgen picture of this condition is characteristic. The shafts of the long bones are short and broad. The epiphyses are overhanging. The hands are stubby. Connective tissue growth into the space between the epiphysis and diaphysis causes retardation of the growth of the shaft. The fibula is longer than the tibia.

Various rarer anomalies of bony development cannot be entered into here because of limitations of space, and because many of them are not generalized throughout the skeleton.

(II) INFECTIONS

Syphilis.—Under this heading we have chosen syphilis, which is the only generalized infection which commonly involves the long bones.

Syphilitic involvement of bones is of importance in infancy and childhood because of the symptoms produced and because roentgenograms of the bones may be of assistance in establishing the diagnosis of syphilis. The bones are involved in a majority of infants with congenital syphilis; usually, but not invariably, roentgenograms can demonstrate this involvement.

Syphilitic lesions of the bones producing symptoms and roentgenographic evidence occur with greatest severity in the first six months of life.

The chief symptoms of syphilis of the bones in infants are due to osteochondritis, which may give rise to fractures through the weakened area at the epiphysis. Such fractures produce pain, crepitation, swelling, tenderness and pseudoparalysis.

From a diagnostic standpoint, the importance of x-raying the long bones of infants suspected of being luetic lies in the fact that roentgenographic evidence of syphilis may be present before the serologic tests for syphilis are positive. However, great caution must be exercised in diagnosing syphilis from roentgenograms in the absence of confirmatory serologic tests.

Late bone lesions of syphilis such as saber shins and gumma will not be discussed.

The x-ray changes are considered in two

stages: those which occur in the newborn and before the third month, and (2) those which occur after the third month.

In the newborn period, the first recognizable changes are a narrow zone 1 to 2 mm. in width in the zones of provisional calcification. This is thought to be the result of the irritative factor of the first lesion, a syphilitic osteochondritis. In the submetaphyseal area, a zone of radiolucency due to decalcification occurs. As the disease progresses, the changes typical of an osteochondritis develop, namely, a ragged irregular appearance at the end of the shaft. In very severe cases, a syphilitic osteomyelitis may develop and this process occurring in the medial portion of the upper ends of the tibiae is pathognomonic.

After the third month, in addition to the above changes, syphilitic periostitis ossificans with its typical onion peel appearance along the shafts becomes manifest. This change may become very extensive in severe, untreated cases.

Active treatment causes marked regression of all of these changes.

(III) ENDOCRINE DISTURBANCES

Hypothyroidism and hypogonadism both produce definite delay in bone growth. No characteristic changes are produced except delay in appearance of ossification centers.

(IV) METABOLIC DISTURBANCES

(1) *Rickets.*—The symptomatology of rickets is too well known to warrant discussion here. The essential features are a weakness of bone, muscles, and ligaments. Bossing of the skull, delay in closure of the fontanelles, asymmetry of the head, costochondral beading, Harrison's groove, protuberant abdomen, umbilical hernia, bowlegs, knock-knees, thickening of wrists and ankles, and constipation are the main symptoms. Roentgenograms are of importance not only in establishing the diagnosis but in demonstrating the efficacy of treatment by demonstrating healing of the bone lesions.

The x-ray changes in this condition are familiar to practically all who treat children. The bones show a generalized loss of calcium, producing an osteoporosis. The trabeculae are coarsened. The cartilages of the epiphyses fail to show the normal ossification centers. The metaphyseal plates at the end of the bones are broad and ill-defined, and there is flaring of the ends. If the child has crawled or walked, there is usually the wine-glass deformity or cupping at the ends of the bone, due to compression. If the condition remains untreated for too long a period of time, bowing of the tibiae with inward rotation of the lower ends results.

After therapy is instituted, the appearance of the bones shows a rapid return to normal. However, dense transverse lines in the ends of the shaft remain as evidence of the previous growth disturbance.

(2) *Scurvy.*—Scurvy appears, as a rule, only in bottle-fed babies whose diet has been deficient in vitamin C. Breast-fed babies are rarely affected. The onset is usually in the second six months of life, although it may appear somewhat earlier or later. The chief manifestations are failure to thrive, irritability, tenderness of the knees, swelling of the knees, swollen and bleeding, purplish gums, hemorrhages into the skin or from mucous membranes, low fever, and anemia. The chief diagnostic findings are tenderness of the knees and purple, swollen, bleeding gums. The diagnosis is established by the history, physical examination, roentgenograms of the long bones, and determination of the cevitamic acid level of the blood. The addition of adequate amounts of vitamin C to the diet, usually in the form of orange juice, is rapidly curative.

Here, again, the x-ray changes are quite familiar to anyone in pediatric practice. The bones present a ground-glass appearance without coarse trabeculae. The metaphyseal plates are broadened, wavy and denser than normal. In the submetaphyseal region, there is a rather wide band of rarefaction, the so-called Trummerfeld's zone, or scurvy line. The cortex of the bones is thin. The epiphyses show a thin white dense edge. Occasionally, after initiation of treatment, subperiosteal hemorrhages become visible due to the presence of calcification within them.

(3) *Xanthomatosis.*—There are several types of xanthomatosis, Hand-Schuller-Christian's syndrome and chronic Gaucher's disease being the most common in pediatric practice.

The xanthomatoses are constitutional disorders of metabolism in which deposition of lipoid fat mixtures occur in various portions of the body, causing granuloma-like accumulations.

Hand-Schuller-Christian's syndrome consists of some or all of the following manifestations: bone defects, especially of the skull; exophthalmos of varying degree, diabetes insipidus, loose

teeth and swollen gums, dwarfism, occasionally a yellow discoloration of the skin, and rarely, yellow to brownish colored eruptions and nodules in the skin and mucous membranes.

The symptoms are due to the formation of lipoid granulomas with consequent pressure and erosion of structures at various sites.

Chronic Gaucher's disease produces some or all of the following manifestations: enlarged spleen, enlarged liver, leukopenia and thrombocytopenia, brownish discoloration of the exposed parts of the skin, hemorrhages, emaciation, skeletal defects, and cuneiform thickening of the conjunctiva near the cornea.

The lesions in Schuller-Christian's disease are entirely due to the replacement of normal bone structure by the lipoid material. Roentgenologically there are noted large irregular, but sharply defined defects in the skull wall and occasionally in the long bones. These lesions show no surrounding area of sclerosis. The sella turcica may be absent due to replacement by the lipoid material. The areas in the skull have been described as map-like.

Gaucher's disease is not so prone to show bone changes as Schuller-Christian's disease. However, there may be present expansion of the lower ends of the shafts and thinning of the cortex.

(v) CHANGES DUE TO CHEMICAL AGENTS

The excessive intake of certain heavy metals therapeutically or accidentally in the growing infant or child results in the deposition of these metals in the zones of growth of the bones. This is noted particularly in lead poisoning and after the administration of phosphorus by mouth, or bismuth intramuscularly.

Radiographs reveal wide bands of metallic density in the ends of the long bones.

(vi) ANEMIAS

Sickle Cell Anemia and Erythroblastic Anemia.—The bone changes in these two anemias are due to regenerative hyperplasia of the marrow with variable widening of the marrow and consequent thinning of the cortex.

In erythroblastic anemia, or Cooley's anemia, there is marked generalized osteoporosis throughout the entire skeleton. The trabeculae of the bones are coarsened. The most characteristic finding, however, is a very pronounced spicule formation over the entire skull, the spicules being perpendicular to the skull wall.

The changes of sickle cell anemia are essentially like those in Cooley's anemia, although not so marked. Children may not show the bone findings as well as adults do. The cortex of the shafts of the long bones is thinned due to the encroachment of hyperplastic marrow. A canalization of the cortex occurs due to hyperplastic marrow invasion of the haversian canals. Occasionally, infarcts occur in these canals, resulting in thickened, irregular areas in the cortex.

CONCLUSIONS

The bone changes in certain common diseases of children have been discussed.

This method of study is recommended in certain generalized diseases in which the diagnosis is doubtful and also in some instances as a prophylactic study to insure treatment in unsuspected conditions before permanent damage has taken place.

A NOTE ON THE EFFECT OF ALPHA-TOCOPHEROL (VITAMIN E) IN HUMAN NUTRITION*

By TOM D. SPIES, M.D.
Birmingham, Alabama
and
RICHARD W. VILTER, M.D.
Cincinnati, Ohio

Nutritional muscular diseases have been reported in rats,[1] guinea pigs,[2] rabbits[3] and dogs[4] on diets low in vitamin E; and a considerable number of studies have been made upon the effect of wheat germ, which contains alpha and beta tocopherols, upon neuromuscular symptoms in experimental animals and human beings. Recently, it was observed independently[5,6] that synthetic alpha-tocopherol (vitamin E) sometimes has a beneficial effect upon muscular disease in human beings. This observation suggests the therapeutic equivalence of synthetic alpha-tocopherol and the "myotrophic" and "neurotrophic" factors present in wheat germ. The present report suggests an effect by synthetic alpha-

*Received for publication May 17, 1940.

*From the Department of Internal Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio, and the Hillman Hospital, Birmingham, Alabama. These studies were aided by grants to the University of Cincinnati from the John and Mary R. Markle Foundation and Anheuser-Busch, Inc.

tocopherol on chronically malnourished human beings.

During the past year, fourteen chronically malnourished patients from the Nutrition Clinic, Hillman Hospital, Birmingham, Alabama, were selected for study. These patients showed no clinical evidence of pellagra, beriberi, or riboflavin deficiency, but complained of extreme weakness, inability to work, loss of appetite, insomnia, aching and cramping sensations of the legs, and burning of the soles of the feet; and three of them experienced roaring sensations in the ears.

Neurologic examination showed coarse tremor of the muscles, diminished vibration sense in the legs, diminished ankle jerks, and a mild degree of hypesthesia in the legs. Three of the fourteen had a macrocytic anemia, with a red count of less than 2,500,000.

Five hundred milligrams of synthetic alpha-tocopherol (Merck) in sterile oil were administered, intramuscularly, to each patient.

Within twenty-four hours, 12 of the 14 patients volunteered the claim of striking improvement in strength and sense of well-being, and for the first time in a long period were able to do a day's work. Two of the patients showed no improvement. In each instance in which improvement occurred, the cramping, burning and aching sensations in the calf muscles disappeared; the roaring sensations in the ears ceased, and muscular tenderness diminished. Eight of the patients, who had been ill for many years, were followed for one month after the first dose of alpha-tocopherol, and maintained their original improvement. This may well be due to the improved diet which they were able to obtain by virtue of the fact that they were able to resume work. The remaining four patients relapsed to the original level of discomfort and weakness at the end of the first week, but showed striking improvement again following the second injection of 500 milligrams of alpha-tocopherol. A slight reticulocyte response in the patients with macrocytic anemia was observed during the first week after the initial injection of alpha-tocopherol, but there was no increase in red count or hemoglobin.

In addition to the fourteen chronically malnourished persons, we treated a case of pernicious anemia in relapse, which was accompanied by posterolateral degenerative disease of the spinal cord and peripheral neuritis. No improvement followed the administration of 500 milligrams of synthetic alpha-tocopherol to this patient and the blood picture was not altered.

SUMMARY

These findings suggest that an injection of synthetic alpha-tocopherol (vitamin E) is effective temporarily in relieving neuromuscular symptoms, roaring sensations in the ears, anorexia, and insomnia of selected persons with malnutrition, but no clinical evidence of pellagra, beriberi, or riboflavin deficiency.

BIBLIOGRAPHY

1. Evans, H. M.; and Burr, G. O.: Development of Paralysis in the Suckling Young of Mothers Deprived of Vitamin E. Jour. Biol. Chem., **76**:273, 1928.
2. Goettsch, M.; and Pappenheimer, A. M.: Nutritional Muscular Dystrophy in the Guinea Pig and Rabbit. Jour. Exper. Med., **54**:145, 1931.
3. Morgulis, S.: Monographie Actualites Scientifigues et Industrielles, p. 75. Paris: Herman & Cie, 1938.
4. Anderson, H. D.; Elvehjem, C. A.; and Gonce, J. E., Jr.: Vitamin E Deficiency in Dogs. Proc. Soc. Exp. Biol. & Med., **42**:750, 1939.
5. Wechsler, I. S.: Recovery in Amyatrophic Lateral Sclerosis Treated with Tocopherols (Vitamin E): Preliminary Report. J.A.M.A., **114**:948, March 16, 1940.
6. Spies, T. D.: The Vitamin B Deficiencies. Transactions and Studies of the College of Physicians, April, 1940. (Read before the College of Physicians of Philadelphia, February 7, 1940.)

Southern Medical Journal
JOURNAL OF THE
SOUTHERN MEDICAL ASSOCIATION

Copyright, Southern Medical Association, 1940. Published monthly by the Southern Medical Association, Empire Building, Birmingham, Alabama. Annual subscription, $4.00. Single copies, 35c each.

Entered as second-class matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

M. Y. DABNEY, M.D., Editor
C. P. LORANZ, Secretary, Treasurer and General Manager

Volume 33 JUNE 1940 Number 6

EDITORIAL DEPARTMENT

SOUTHERN MEDICAL ASSOCIATION
Thirty-Fourth Annual Meeting
Louisville, Kentucky, November 12-15, 1940

THE LOUISVILLE MEETING

HOBBY AND ART EXHIBIT

"No man is really happy or safe without a hobby and it makes precious little difference what the outside interest may be."—*Sir William Osler.*

Many physicians indulge themselves in a hobby that invades the fields of fine arts, and frequently their excellent work is not only self-satisfying but interesting enough to display to their friends. Consequently, this year the Southern Medical Association is sponsoring a HOBBY SHOW to exhibit pictures, handicraft and anything its members may wish to present.

The exhibit will be non-competitive and open to physicians who are members of their state and county medical society in the territory from which the Southern Medical Association draws its membership. The Hobby Exhibit will be placed near the Scientific Exhibit at the Louisville meeting. Any physician interested, who has a hobby to exhibit, is requested to write for a special form on which to give the Hobby Committee the information needed about the display. Forms may be secured from Dr. Jesshill Love, Chairman of the Hobby Committee, 1010 Brown Building, Louisville, Kentucky, or the Southern Medical Association, Empire Building, Birmingham, Alabama.

POTASSIUM AND TEMPERATURE

One thinks of an increase of temperature as depending upon increased oxidation within the body, and thus upon consumption of the basic fuel of the body, carbohydrate. That there can be no carbohydrate metabolism without considerable shifting of mineral as well as vitamin elements within the body, is shown in various ways. Potassium is one of the less studied elements in the blood, which appears to vary considerably with changes in body temperature.

This alkaline earth element is intimately concerned in muscle activity. Contraction depletes the muscle of potassium and raises the level of potassium in the blood plasma. Anesthetics lower plasma potassium, and this is to be expected since they decrease muscular activity. But the decrease in plasma potassium may be prevented or converted to an increase if one administers a metabolic stimulant such as dinitrophenol, which, like thyroid extract, raises the basal metabolism.[1]

A cold environment, according to Brewer,[1] of the University of Pennsylvania, brings about an increase in metabolism and in blood potassium of experimental animals. Dinitrophenol in appropriate dosage increases metabolism, body temperature and plasma potassium. This occurs if the medulla of the adrenal gland has been removed and the level of blood sugar remains unaltered; it happens under anesthesia, in the absence of muscular activity, and after the liver has been removed. Within a certain range of temperatures of the animals used, there seemed to be a direct relationship between blood potassium level and body temperature.

Changes in potassium utilization are characteristic of Addison's disease (hypo-adrenal corticism), and in this condition the patient is very sensitive to potassium. He requires large amounts of sodium and a crisis of the disease may be brought about by administration of potassium. Presumably in the opposite condition of Addison's disease, that is, in hyperadrenal corticism, he would require large amounts of potassium, and sodium would be toxic, as it is believed to be in certain pregnancy toxemias.

One wonders as to the level of potassium in hyperthyroid disease, since dinitrophenol, which reacts physiologically much like dessicated thy-

1. Brewer, George: Relation of Plasma Potassium Level to Metabolic Activity. Amer. Jour. Physiol., **129**:245 (May) 1940.

roid gland, raises the plasma potassium. This may be an effect worthy of note in thyroid crises. High plasma potassium, if it exists in thyroid crises, would be apt in itself to cause serious symptoms. Determination of the blood potassium height in terminal high temperatures of any etiology might provide useful information.

It is of interest that this mineral element varied directly in the animals studied with the temperature of the animal and not with its activity or ration.

LARYNGEAL PAPILLOMATA AND ESTROGENS

Some years ago, Lewis showed that gonorrheal vulvovaginitis in young children, which was very difficult to cure before puberty, could be controlled rather promptly by parenteral injections of the ovarian follicle hormone, the estrogenic hormone. This product caused a thickening of the vaginal lining, which was usually followed by eradication of the infection. Local applications of the hormone were later shown to result in thickening of the vaginal mucosa of young girls.

Papillomas are common benign tumors of the larynx which are frequently recurrent and difficult to treat in young children. They tend to spontaneous arrest at puberty. There is some evidence that they are infectious and caused by a filterable virus.[1]

The very obvious differences in male and female voices, the voice changes of the boy at puberty, and the fact that malignancy of the larynx is much more frequent in men than in women, would seem to place laryngeal structure under the influence or control of the gonads.

It was attempted in 1938, by injection of testosterone, to bring about puberty and recession of laryngeal papillomata in a young boy, but without success. Broyles,[1] of Johns Hopkins Hospital Department of Laryngology, has recently treated five cases by weekly local applications of an estrogenic hormone in oil, which was sprayed directly into the larynx. The papillomatous growths disappeared without further recurrence in all cases, and there were no secondary sex changes. The treatment seemed to be a very simple and a remarkably effective one for a hitherto intractable condition.

1. Broyles, Edwin N.: Treatment of Laryngeal Papilloma in Children with Estrogenic Hormone. Bull. Johns Hopk. Hosp., **66**:319 (May) 1940.

It is most interesting to note reports that this hormone, which is believed to have a definite relationship to the establishment of mammary carcinoma in several types of animals, apparently controlled a type of abnormal growth in the larynx.

AN UNSCIENTIFIC MOVIE

Word has been passed that Paramount Pictures is preparing a motion picture entitled "Triumph Over Pain" depicting Morton, the Boston dentist, as the discoverer of ether anesthesia.

Dr. Crawford W. Long, of Jefferson, Georgia, began the use of sulfuric ether as a general anesthetic four years before Morton. Long used it in 1842; Morton not until 1846. That fact has been recognized by medical investigators and by medical organizations, and officially by the Southern Medical Association in 1921 and 1922. Long's priority is now so well established that the United States Postal Department, after going into the matter very carefully and after having consulted authorities on medical history, cast aside the false claims of Morton and placed the picture of Long on the new commemorative stamp that is at present for sale in most postoffices of this country.

Morton possessed the earmarks of a quack in that he attempted to patent ether, which would have interfered with spread of its use among the poor, and he tried to secure for himself a Government pension for a service that he had never rendered. The memory of a great man should not be deprived of its just recognition and displaced by one unworthy to tie his shoe laces. The tremendous publicity that would result from false propaganda of this nature, through an elaborate and expensively prepared moving picture on Morton as the discoverer of ether anesthesia, could hardly be corrected in a generation.

Lessons taught in the movies remain longer than those taught at school, and the films have become such a tremendous influence upon public opinion, taste and information, and the historic and scientific movie so popular, that one feels that there should actually be some penalty for motion picture distortions of history. One's first impulse is to think that really there should be a law against it.

Use of a Government bureau for this purpose would provide troublesome red tape, and would no doubt be worse than the ill. The agency for preventing falsification of historic facts must be enlightened public opinion, acting upon those

directing the picture industry. The public, to enlighten itself, can do little better than to listen to information obtainable from experts.

A radio skit has already been broadcast which gave Morton credit for this work. Informed physicians should make every effort to express themselves on the subject to the President of Paramount.

TWENTY-FIVE YEARS AGO

From Journals of 1915

Crystalline Thyroxin.[1]—"* * * the compound containing iodine, the presence of which as a normal constituent of the thyroid was foretold by Baumann nineteen years ago, has been isolated in pure crystalline form, and further it has been shown that this compound is the substance in the thyroid which is responsible for the physiological activity of the gland. * * * Administration produces * * * a rapid increase in pulse rate and vigor and increase in metabolism and nervous irritability."

Accidents in America.[2]—In the United States of America human life is cheap and industrial accidents frequent. An estimate by Mr. T. J. Riley in the Bulletin of the Department of Public Health of New York City places the number of deaths by such accidents at nearly 35,000 per annum. It is calculated that the total number of both fatal and non-fatal industrial accidents must be about 700,000 a year.

Diet of World War Prisoners in Germany.[3]—Prisoners in the German camps receive a diet containing 2,700 calories a day on the average. The menu for one day was bread 10 oz., potatoes 1 lb. 4 oz., pork 3½ oz., dry vegetables 1¼ oz., margarine 1.8 oz., preserved vegetables 3¼ oz.—2,899 calories at a cost of 7 d. Bread is the only food given in solid form; everything else is boiled into a thick soup which is served at all meals * * * by giving the food as a soup there is no waste. * * * What the nutritive value of the war bread is we do not know. * * * German war meal contains 10 per cent of ash and practically no starch, and would appear to be ground up straw used as a diluent. * * * A package dispatched from this country by post usually takes from ten days to three weeks to reach a prison camp.

A Century After Waterloo.[4]—One hundred years have passed away since the battle of Waterloo was fought on June 18, 1815, and Napoleon's power finally crushed by the British army under Wellington, aided by that of Prussia under Bluecher. After the lapse of a century we see the same combatants, differently grouped as allies, again locked in a life and death struggle. The total forces engaged on both sides, the number of casualties, the duration of the contest are now all upon a scale compared to which Waterloo seems but a skirmish. The battle of Waterloo was lost and won in one long summer day, or if we include the preliminary battle of Quatre Bras, in three days. The number engaged were about 70,000 on each side, the British and allied casualties about 27,000, the French about the same. These numbers are small compared to the first battle of Ypres, fought through October and November of last year, which lasted some six weeks, and in which the casualties on both sides together are said to have amounted to about half a million. Yet Waterloo settled the destinies of Europe for about half a century. Can the present titanic struggle do more?

1. Kendall, E. C.: The Isolation in Crystalline Form of the Compound Containing Iodine Which Occurs in the Thyroid. J.A.M.A., **64**:2042 (June 19) 1915.

2. Editorial, Industrial Accidents in America. Lancet, **188**: 1191, 1915.

3. Editorial, Diet of Prisoners in Germany. Brit. Med. Jour., p. 1014, June 12, 1915.

4. Waterloo. Brit. Med. Jour. p. 1050, June 19, 1915.

Book Reviews

Elmer and Rose Physical Diagnosis. Revised by Harry Walker, M.D., F.A.C.P., Associate Professor of Medicine, Medical College of Virginia, Richmond, Virginia. Eighth Edition. 792 pages, illustrated. St. Louis: The C. V. Mosby Company, 1940. Cloth $8.75.

This revision is made by Dr. Harry Walker, who has added an introduction which summarizes the history taking and the recording of the physical examination. The chapters have been rearranged so that they are in the sequence normally followed in making an examination of the patient. Some of the older illustrations have been deleted and a few new ones inserted. The content has been changed in accord with new investigations. An excellent textbook in its field.

A Textbook of Physiology. By William D. Zoethout, Ph.D., Professor of Physiology in the Chicago College of Dental Surgery (Loyola University), and W. W. Tuttle, Ph.D., Professor of Physiology, College of Medicine, State University of Iowa. Seventh Edition. 743 pages, illustrated. St. Louis: The C. V. Mosby Company, 1940. Cloth $4.50.

This is a popular textbook of physiology and well adapted to the needs of the college student. It has been kept up to date by frequent revisions. This edition introduces Dr. W. W. Tuttle as a co-author. A few new illustrations have been added and the book has been increased in size by about fifty pages.

An Introduction to Gastro-Enterology. Being the Third Edition of the Mechanics of the Digestive Tract. By Walter C. Alvarez, Professor of Medicine, University of Minnesota, The Mayo Foundation. 778 pages, illustrated. New York: Paul B. Hoeber, Inc., 1940. Cloth $10.00.

This third edition has been greatly enlarged in scope and size. While it is a little too large for the book shelves of similar works, the format is excellent. One is fascinated by the beautiful printing and literary form. An unusual, but acceptable feature, is found in the pictures of a large group of contemporaneous scientists, which is a tribute to these living men.

The first edition was entitled "The Mechanics of the Gastro-Intestinal Tract," which described in detail the peristaltic movement of the alimentary tract on the

basis of the gradient theory. In this edition, corroborative evidence of the sound physiologic basis for this theory is convincingly presented. In addition it is an excellent book on experimental physiology, giving rational explanations of the various symptoms usually indicative of disturbed physiology. The mechanics of the gallbladder, the modus operandi of gastro-enterostomy and other topics of special interest to the gastroenterologists are presented.

The concluding section is an exhaustive list of references on this subject, with valuable suggestions for the young medical specialist on how to read for the greatest profit. It is a monumental work by an eminent scientist, and will always be considered a medical classic.

Modern Diabetic Care, Including Instructions in the Diet and the Use of the Old and New Insulins. By Herbert Pollack, A.B., Ph.D., M.D., Instructor in Clinical Medicine, Cornell Medical College. 216 pages. New York: Harcourt, Brace & Co., 1940. Cloth $2.00.

This book gives the history of diabetes and the discovery of insulin. Special emphasis is placed on the use of protamine zinc insulin. Its advantages are given. The author brings out the fact that a diabetic on a controlled diet and protamine zinc is in no sense a social outcast. By taking protamine zinc insulin in the privacy of his home before breakfast he will not be embarrassed by the jeers of his friends and can live a normal life throughout the day.

The book is written for both patient and physician, but primarily for the former, as very little technical language is used.

The writer points out that it is seldom necessary to weigh a diabetic's diet, and that the diet should be selected from the usual foods for non-diabetics. The patient must be taught exactly which foods he can eat and the amounts.

An excellent discussion is given on the hygienic care of the diabetic.

The chapters on complications in diabetes and surgery and pregnancy in diabetes are instructive and well worth reading.

The latter part of the book is taken up with very helpful diet suggestions.

Artificial Pneumothorax: Its Practical Application in the Treatment of Pulmonary Tuberculosis. Contributions by Saranac Lake Physicians to the Studies of the Trudeau Foundation. Editorial Committee, Edward N. Packard, M.D., John N. Hayes, M.D., and Sidney F. Blanchet, M.D. Foreword by E. R. Baldwin, M.D. 300 pages, illustrated. Philadelphia: Lea & Febiger, 1940. Cloth $4.00.

Pneumothorax therapy is one of the common procedures in medicine about which very few books have been written. This book by physicians of the Trudeau Foundation fills a long-felt need. It is a thoroughly authoritative and practical monograph.

The technic and procedure of pneumothorax, initial and refills, are described in detail. Indications, contraindications and complications are well discussed. Accidents during pneumothorax and their management are given a full chapter. When to discontinue pneumothorax, which is always a serious and difficult decision, is given thorough consideration. Every chapter is informative and helpful. The physician treating tuberculosis will find this book invaluable.

A Topographic Atlas for X-Ray Therapy. By Ira I. Kaplan, M.D., Director, Radiation Therapy Department, Bellevue Hospital, Professor of Surgery, New York University Medical College; and Sidney Rubenfeld, M.D., Associate Visiting Radiation Therapist, Bellevue Hospital, Instructor in Surgery, New York University Medical College, New York City. 120 pages, illustrated. Chicago, Illinois: The Year Book Publishers, Incorporated, 1939. Cloth $4.00.

This topographic atlas for x-ray therapy is the first of its kind to be published. It contains 55 plates showing the visible anatomical landmarks; the palpable internal landmarks; the organ or part to be irradiated; and the position of the treatment cone in order to give the most efficient dosage with the least harm to surrounding normal tissues. Accompanying each plate there is a convenient printed outline giving the anatomic landmarks, position of treatment cone and direction of treatment cone. There has long been a need for a descriptive atlas in which radiologists may tell at a glance the average anatomic position of organs and tissues to be treated, and this volume will be of invaluable aid for such a purpose. It is also a splendid guide in teaching.

Oxford Monographs on Diagnosis and Treatment. Volume V. The Diagnosis and Treatment of Chronic Diseases of the Respiratory Tract, with Especial Reference to the Lesions of the Trachea, Bronchi, Lungs, Pleura and Diaphragm. By Elmer H. Funk, M.D. Revised by Burgess Gordon, M.D., Medical Director and Physician-in-Charge, Department for Diseases of the Chest, Jefferson Hospital, Philadelphia; Associate Professor of Medicine, Jefferson Medical College. (Supplement.) New York: Oxford University Press, 1939.

These new pages for insertion in the Oxford Monographs embody the latest diagnostic procedures and methods of treatment for chronic diseases of the respiratory tract.

Medical Climatology: Climatic and Weather Influences in Health and Disease. By Clarence A. Mills, Ph.D., M.D., Professor of Experimental Medicine, University of Cincinnati. 296 pages, illustrated. Springfield, Illinois: Charles C. Thomas, Publisher, 1939. Cloth $4.50.

If the reader is not too critical, he will in reading this interesting exposition come to the conclusion that growth, development, fertility, metabolism, body resistance, mental function, vascular disease, dental caries and various other body functions are dependent upon climate. The author defines climate as "average conditions over many years or decades," while weather is "short-cycle conditions." He states that children conceived in June and born in February or March will have longer life and a better chance of success. In the same manner it is suggested that we are entering upon a period of world warmth such as was seen during the centuries of the Dark Ages and that there is at present a recession in man. It is a book which will excite more study in this field.

Nomenclature and Criteria for Diagnosis of Diseases of the Heart. By the Criteria Committee of the New York Heart Association. Arthur C. DeGraff, M.D.; Clarence E. De La Chapelle, M.D.; Cary Eggleston, M.D.; Charles E. Kossman, M.D.; Robert L. Levy, M.D.; John B. Schwedel, M.D.; Harold E. B. Pardee, M.D., Chairman. Fourth Edition. New York: New York Heart Association, a Division of New York Tuberculosis and Health Association, Inc., 1939.

For a number of years the American Heart Association has been attempting to educate the medical profession in regard to heart disease. One of the most important steps along this line has been the publication from time to time of the volume which now appears in its fourth edition. The first part of the book deals with nomenclature and includes a comprehensive summary of the various types of heart disease as seen from the standpoint of etiology, physiology and anatomy. There is then a brief discussion of the criteria which are necessary in order to make a diagnosis of the different types of heart disease. These discussions are necessarily brief because the whole purpose of the book is to make it inexpensive and readily available as a source of reference. This purpose has been admirably achieved in most respects. Although such a small book presenting material in condensed form cannot take the place of the more complete volumes dealing with the heart, this little book is nevertheless a highly useful one not only for the internist but for the general practitioner and the student as well.

The Heart-Sounds in Normal and Pathological Conditions. By Oscar Orias, Director of the Institute of Physiology, and Professor Orias, Director of the Institute of Medical Sciences, Cordoba (Argentine), and Eduardo Braun-Menendez, M.D., Director of Cardiological Investigations in the Institute of Physiology, Faculty of Medical Science, Buenos Aires. 258 pages, illustrated. New York: Oxford University Press, 1939. Cloth, $4.75.

In this book the authors deal with a study of the heart sounds by graphic methods. This investigation has lasted over a period of a number of years and has evidently been carried out with great care. The authors emphasize that in order to interpret tracings of the heart sounds it is necessary to carry these out not only simultaneously with the electrocardiogram, but also, and particularly, with tracings of the venous pulse. For anyone who wants to make phonocardiographic studies this book is valuable. Even for physicians who do not care to use this method the book is also useful, for its perusal will elucidate many of the features in regard to the heart sounds which are constantly puzzling clinicians. Discussions of the third heart sound, the various types of gallop, the opening snap of the mitral valve and certain confusing aspects of the murmur of mitral stenosis are particularly good. The discussion of the heart sounds in the various types of heart block is also excellent, although in the opinion of the reviewer the authors are inclined to place too much stress on muscular origin of sounds and do not emphasize sufficiently the importance of recent work pointing toward the heart valve as the chief and possibly the sole source of the sound. This objection is not sufficient to diminish the value of the book. Any clinician who studies it carefully will be better able to interpret the things he hears at the bedside. Much of the material with which the authors deal represents original work and hence cannot be found elsewhere. This is probably the best discussion of the heart sounds which has ever been written.

Cardiovascular-Renal Disease: A Clinicopathologic Correlation Study Emphasizing the Importance of Ophthalmology Based on Material Awarded the Frank Billings Gold Medal at the Scientific Exhibit of the Annual Meeting of the American Medical Association, San Francisco, June 1938. By Lawrence W. Smith, M.D., Professor of Pathology, Temple University School of Medicine; Edward Weiss, M.D., Professor of Clinical Medicine, Temple University School of Medicine; Walter I. Lillie, M.D., Professor of Ophthalmology, Temple University School of Medicine; Frank W. Konzelmann, M.D., Professor of Clinical Pathology, Temple University School of Medicine; Edwin S. Gault, M.D., Associate Professor of Pathology, Temple University School of Medicine. 227 pages, illustrated. New York: D. Appleton-Century Company, Inc., 1940. Cloth, $4.50.

This book deals with various aspects of hypertension and nephritis. The authors have managed to cover this broad subject adequately within the space of relatively few pages. Beginning with a general discussion of the clinical features of hypertension and a consideration of the pathologic point of view as well as an approach to the problem from the statistical aspect, the subjects of essential hypertension, renal arteriosclerosis, nephritis, nephrosis and pyelonephritis are discussed. This is a field in which rapid advances are being made and this book will bring the reader well up to date in regard to them. There are many excellent photographs, particularly those dealing with the pathology of the kidneys and with ophthalmoscopic pictures. Throughout the book the importance of ophthalmoscopy is emphasized and the numerous excellent reproductions of ophthalmoscopic abnormalities will serve to familiarize the reader with this important method of examination of the vascular system. The book can be strongly recommended.

Manual of Fractures, Dislocations and Epiphyseal Separations. By Harry C. W. S. de Brun, M.D., F.A.C.S., Adjunct Professor of Surgery, New York Polyclinic Medical School and Hospital. 468 pages, illustrated. Chicago: The Year Book Publishers, Inc., 1940. Cloth, $3.00.

The general principles of treatment of fractures have not changed greatly, according to de Brun. However, the types of fractures caused by industrial and traffic accidents and military combat have made it necessary to alter technical procedures.

For this reason, books on treatment of fractures and dislocations must be increasingly comprehensive, and the subject cannot be considered at all in such a small volume as this.

This very brief book contains few illustrations of every day common sense practical methods of treatment. Most of the illustrations show apparatus secured from splint manufacturers and applicable in very select and rare cases.

Book Reviews continued on page 671

OFFICERS 1939-1940

The following is a complete roster of the officers of the Southern Medical Association for 1939-1940, and of associations meeting conjointly with the Southern Medical Association.

President—Dr. Arthur T. McCormack, Louisville, Kentucky.

President-Elect—Dr. Quitman U. Newell, St. Louis, Missouri.

First Vice-President—Dr. W. L. Williamson, Memphis, Tennessee.

Second Vice-President—Dr. E. W. Bertner, Houston, Texas.

Secretary-Manager (Secretary, Treasurer and General Manager)—Mr. C. P. Loranz, Birmingham, Alabama.

Editor of Journal—Dr. M. Y. Dabney, Birmingham, Alabama.

Associate Editor of Journal—Mrs. Eugenia B. Dabney, Birmingham, Alabama.

Councilors—Dr. Vincent W. Archer, Chairman, Charlottesville, Virginia; Dr. E. W. Rucker, Jr., Birmingham, Alabama; Dr. S. J. Wolfermann, Fort Smith, Arkansas; Dr. Oscar B. Hunter, Washington, D. C.; Dr. Luther W. Holloway, Jacksonville, Florida; Dr. Marion C. Pruitt, Atlanta, Georgia; Dr. E. L. Henderson, Louisville, Kentucky; Dr. Lucien A. LeDoux, New Orleans, Louisiana; Dr. J. Mason Hundley, Jr., Baltimore, Maryland; Dr. William H. Anderson, Booneville, Mississippi; Dr. Alphonse McMahon, St. Louis, Missouri; Dr. Hamilton W. McKay, Charlotte, North Carolina; Dr. Robert M. Anderson, Shawnee, Oklahoma; Dr. Kenneth M. Lynch, Charleston, South Carolina; Dr. Horton Casparis, Nashville, Tennessee; Dr. Guy F. Witt, Dallas, Texas; Dr. R. J. Wilkinson, Huntington, West Virginia. Executive Committee: Dr. Archer, Chairman, Dr. McMahon and Dr. Henderson.

Board of Trustees (All are Past-Presidents)—Dr. Hugh Leslie Moore, Chairman, Dallas, Texas; Dr. H. Marshall Taylor, Jacksonville, Florida; Dr. Fred M. Hodges, Richmond, Virginia; Dr. Frank K. Boland, Atlanta, Georgia; Dr. J. W. Jervey, Greenville, South Carolina; Dr. Walter E. Vest, Huntington, West Virginia.

Section on Medicine—Dr. Henry G. Rudner, Chairman, Memphis, Tennessee; Dr. W. G. Reddick, Vice-Chairman, Dallas, Texas; Dr. Roy H. Turner, Secretary, New Orleans, Louisiana.

Section on Pediatrics—Dr. Harvey F. Garrison, Chairman, Jackson, Mississippi; Dr. James W. Bruce, Vice-Chairman, Louisville, Kentucky; Dr. Warren W. Quillian, Secretary, Coral Gables, Florida.

Section on Gastroenterology—Dr. Chauncey W. Dowden, Chairman, Louisville, Kentucky; Dr. James L. Borland, Vice-Chairman, Jacksonville, Florida; Dr. Donovan C. Browne, Secretary, New Orleans, Louisiana.

Section on Pathology—Dr. Roy R. Kracke, Chairman, Emory University, Georgia; Dr. A. J. Miller, Vice-Chairman, Louisville, Kentucky; Dr. R. H. Rigdon, Secretary, Memphis, Tennessee.

Section on Neurology and Psychiatry—Dr. Spafford Ackerly, Chairman, Louisville, Kentucky; Dr. David C. Wilson, Vice-Chairman, Charlottesville, Virginia; Dr. Theodore A. Watters, Secretary, New Orleans, Louisiana.

Section on Radiology—Dr. Ralph E. Myers, Chairman, Oklahoma City, Oklahoma; Dr. David Y. Keith, Vice-Chairman, Louisville, Kentucky; Dr. W. R. Brooksher, Secretary, Fort Smith, Arkansas.

Section on Dermatology and Syphilology—Dr. Howard Hailey, Chairman, Atlanta, Georgia; Dr. A. B. Loveman, Vice-Chairman, Louisville, Kentucky; Dr. John H. Lamb, Secretary, Oklahoma City, Oklahoma.

Section on Allergy—Dr. Homer E. Prince, Chairman, Houston, Texas; Dr. Marion T. Davidson, Vice-Chairman, Birmingham, Alabama; Dr. Clarence K. Weil, Secretary, Montgomery, Alabama.

Section on Surgery—Dr. J. M. T. Finney, Jr., Chairman, Baltimore, Maryland; Dr. Claude J. Hunt, Vice-Chairman, Kansas City, Missouri; Dr. J. A. Crisler, Jr., Secretary, Memphis, Tennessee.

Section on Bone and Joint Surgery—Dr. J. Hiram Kite, Chairman, Atlanta, Georgia; Dr. F. Walter Carruthers, Vice-Chairman, Little Rock, Arkansas; Dr. Guy W. Leadbetter, Secretary, Washington, D. C.

Section on Gynecology—Dr. John F. Lucas, Chairman, Greenwood, Mississippi; Dr. E. C. Hamblen, Vice-Chairman, Durham, North Carolina; Dr. W. O. Johnson, Secretary, Louisville, Kentucky.

Section on Obstetrics—Dr. Robert M. Anderson, Chairman, Shawnee, Oklahoma; Dr. Joseph W. Reddoch, Vice-Chairman, New Orleans, Louisiana; Dr. R. A. White, Secretary, Asheville, North Carolina.

Section on Urology—Dr. Rex E. Van Duzen, Chairman, Dallas, Texas; Dr. Hubert K. Turley, Vice-Chairman, Memphis, Tennessee; Dr. Grayson Carroll, Secretary, St. Louis, Missouri.

Section on Proctology—Dr. Emmett H. Terrell, Chairman, Richmond, Virginia; Dr. Granville S. Hanes, Vice-Chairman, Louisville, Kentucky; Dr. Frederick B. Campbell, Secretary, Kansas City, Missouri.

Section on Railway Surgery—Dr. Edgar F. Fincher, Chairman, Atlanta, Georgia; Dr. J. J. Brandabur, Secretary, Huntington, West Virginia.

Section on Ophthalmology and Otolaryngology—Dr. Harvey B. Searcy, Chairman, Tuscaloosa, Alabama; Dr. W. Likely Simpson, Chairman-Elect, Memphis, Tennessee; Dr. Albert L. Bass, Vice-Chairman, Louisville, Kentucky; Dr. L. Chester McHenry, Secretary, Oklahoma City, Oklahoma.

Section on Anesthesia—Dr. R. Douglas Sanders, Chairman, Louisville, Kentucky; Dr. George S. Mechling, Vice-Chairman, Oklahoma City, Oklahoma; Dr. Merrill C. Beck, Secretary, New Orleans, Louisiana.

Section on Medical Education and Hospital Training—Dr. Robert U. Patterson, Chairman, Oklahoma City, Oklahoma; Dr. O. W. Hyman, Vice-Chairman, Memphis, Tennessee; Dr. Harvey B. Haag, Secretary, Richmond, Virginia.

Section on Public Health—Dr. W. B. Grayson, Chairman, Little Rock, Arkansas; Dr. L. M. Graves, Vice-Chairman, Memphis, Tennessee; Dr. Henry C. Ricks, Secretary, Jackson, Mississippi.

American Public Health Association, Southern Branch (meeting conjointly with Southern Medical Association)—Dr. G. Foard McGinnes, President, Memphis, Tennessee; Dr. Carl V. Reynolds, First Vice-President, Raleigh, North Carolina; Mr. James H. Stephens, Second Vice-President, Columbia, South Carolina; Miss Ruth A. Heintzelman, Third Vice-President, Washington, D. C.; Dr. P. E. Blackerby, Secretary-Treasurer, Louisville, Kentucky.

National Malaria Committee (meeting conjointly with Southern Medical Association)—Dr. L. O. Howard, Honorary Chairman, Washington, D. C.; Mr. W. G. Stromquist, Chairman, Chattanooga, Tennessee; Dr. J. N. Baker, Chairman-Elect, Montgomery, Alabama; Mr. John H. O'Neill, Vice-Chairman, New Orleans, Louisiana; Dr. Mark F. Boyd, Secretary-Treasurer, Tallahassee, Florida.

American Society of Tropical Medicine (meeting conjointly with Southern Medical Association)—Dr. L. L. Williams, Jr., President, Bethesda, Maryland; Dr. Thomas T. Mackie, President-Elect, New York, New York; Dr. Malcolm H. Soule, Vice-President, Ann Arbor, Michigan; Dr. E. Harold Hinman, Secretary-Treasurer, Wilson Dam, Alabama; Dr. Charles F. Craig, Editor, San Antonio, Texas. *American Academy of Tropical Medicine* (meeting conjointly with American Society of Tropical Medicine)—Dr. Chas. S. Butler, President, Bristol, Tennessee; Dr. Marshall A. Barber, Vice-President, Boston, Massachusetts; Dr. Ernest Carroll Faust, Secretary, New Orleans, Louisiana; Dr. Thomas T. Mackie, Treasurer, New York, New York.

Southern Association of Anesthetists (meeting conjointly with Southern Medical Association)—Dr. T. L. Tidmore, President, Atlanta, Georgia; Dr. R. Douglas Sanders, President-Elect, Louisville, Kentucky; Dr. C. E. Stiadel, Vice-President, St. Louis, Missouri; Dr. Dougal M. Dollar, Secretary-Treasurer, Louisville, Kentucky.

Mississippi Valley Student Health Association (meeting conjointly with Southern Medical Association)—Dr. R. M. Powell, President, Knoxville, Tennessee; Dr. C. B. Mitchell, Vice-President, State College, Mississippi; Dr. Ruby H. Paine, Secretary-Treasurer, Berea, Kentucky.

Women Physicians of the Southern Medical Association—Dr. Nina Fay Calhoun, Chairman, Dallas, Texas; Dr. Miriam M. Drane, Vice-Chairman, Memphis, Tennessee; Dr. Laura M. Hobbs, Secretary, Miami, Florida.

Woman's Auxiliary to the Southern Medical Association—Mrs. Charles P. Corn, President, Greenville, South Carolina; Mrs. M. Pinson Neal, President-Elect, Columbia, Missouri; Mrs. L. S. Thompson, First Vice-President, Dallas, Texas; Mrs. Eustace A. Allen, Second Vice-President, Atlanta, Georgia; Mrs. H. V. Thomas, Recording Secretary, Clarksburg, West Virginia; Mrs. J. W. Bell, Corresponding Secretary, Walhalla, South Carolina; Mrs. K. W. Cosgrove, Treasurer, Little Rock, Arkansas; Mrs. W. T. Braun, Historian, Memphis, Tennessee; Mrs. W. H. Anderson, Parliamentarian, Booneville, Mississippi.

Book Reviews

Continued from page 669

Treatment of War Wounds and Fractures with Special Reference to the Closed Method as Used in the War in Spain. By J. Trueta, M.D., Late Director of the Department of Surgery, General Hospital of Catalonia, Barcelona. With a Foreword by H. Winnett Orr, M.D., F.A.C.S. 146 pages, illustrated. New York: Paul B. Hoeber, Inc., 1940. Cloth $2.50.

This book is a manual of the author's personal experience in 1,073 cases of open limb fractures during 30 months' continuous treatment of war casualties, including the immediate surgical treatment of casualties in 300 air raids in the recent Spanish War. In general, he advocates early thorough soap and water washing, debridement, adequate drainage, excision of foreign organic matter, reduction of fragments by traction and immediate immobilization with plaster according to the method of Orr. He believes that the plaster limits sepsis and destroys invading infection by producing a mixture of organisms on the wound which, by their mutual antagonism, prevent the victory of any one group. Wounds with an already established cellulitis or an anaerobic infection are the only ones not treated by the Orr method.

This report is well written, easy to read, and very interesting. It seems particularly apropos in face of the increasing sphere of the wars now going on.

The Hypothalamus and Central Levels of Autonomic Function. Proceedings of the Association December 20 and 21, 1939, New York. 980 pages, illustrated. Baltimore: The Williams & Wilkins Company, 1940. Cloth $10.00.

This is the twentieth volume of the research publications of the Association for Research in Nervous and Mental Disease. It consists of 35 papers contributed by members of the Association at its annual meeting, December 20, 21, 1939, in New York City, as a symposium concerned with the hypothalamus and central levels of autonomic function. As a wide discrepancy in hypothalamic terminology exists with three distinct terminological systems in use, it was found necessary to draw up a standard terminology and circulate it to all contributors to this volume prior to the meeting. In addition an atlas was compiled to be used with the standard terminology. The precis of terminology with the atlas are found in the volume.

The volume is divided into three parts: anatomy, physiology and clinical symposium. In the anatomical division papers are presented dealing with embryology; comparative anatomy; secretory cells within the hypothalamus; nuclear arrangement and chief connections; and angio-architecture. The group of papers concerned with physiology discuss the relation of the hypothalamus to cardiovascular regulation; body temperature; pilomotor regulation; water, fat and carbohydrate metabolism; gonadotropic functions of the hypophysis; sexual behavior; gastro intestinal functions; vesical activity; sleep; and somatic responses. The clinical symposium discusses changes in the hypothalamus in organic disease; tumors; personality and emotional disorders; cell changes in hypothalamus in major psychosis; temperature disturbances of man; surgery of the hypothalamus; and medical syndromes.

The evidence presented demonstrates that the hypothalamus plays an important role in vegetative functions, in emotional regulation, and probably in personality development; that it is the chief center for the integration of autonomic regulation of body temperature; that it serves to integrate pilomotor activity with other manifestations of fear, rage, thermal regulation and probably sexual excitement; that the anterior hypothalamus is vital to heat loss reflexes, and is the seat of osmotic pressure and specific gravity responses to environmental temperature; that it influences fat metabolism and has an important influence on all gastro-intestinal activity; that it plays an important role in sleep regulation and influences all functions of the anterior pituitary gland. In addition there is a level of integration of somatic activity in the hypothalamus. The data presented strongly suggest that the hypothalamus is one of a series of stations concerned with autonomic function, with the emotions, and to a lesser extent intellect, personality and somatic activity.

This is an exceedingly stimulating symposium and should be of great interest to physiologists and to all men in medicine interested in clinical physiologic problems.

Virus and Rickettsial Diseases, with Especial Consideration of Their Public Health Significance. A Symposium held at the Harvard School of Public Health, June 12-17, 1939. 997 pages. Cambridge, Massachusetts: Harvard University Press, 1940. Cloth $6.50.

This book is composed of 34 papers which were given in June, 1939, at a symposium on this subject conducted by the Harvard School of Public Health. The first four papers are concerned with the general aspects of viruses, epidemiological, physical and chemical, immunological and insect vectors. The remaining 30 chapters deal with variola, vaccine virus and vaccinia, measles, mumps, dengue fever, lymphogranuloma inguinale, absorption of materials from respiratory tract, human and swine influenza, canine distemper, psittacosis, poliomyelitis, a tentative classification of diseases of the central nervous system with a consideration of certain epidemic types of encephalitis, rabies, equine encephalomyelitis, lymphocytic choriomeningitis, louping-ill, yellow fever, and lastly a general survey, diagnosis, classification, clinical features, epidemiology and immunity of the rickettsial diseases. These subjects have been covered by the following authors: W. L. Aycock, K. D. Blackfan, H. D. Chope, C. K. Drinker, R. C. Eley, J. F. Enders, L. D. Fothergill, J. E. Gordon, R. A. Kelser, C. F. McKhann, J. R. Mote, J. H. Mueller, N. A. Nelson, H. Pinkerton, E. S. Robinson, R. A. Ross, F. F. Russell, A. W. Sellards, J. S. Simmons, C. Wesselhoeft, S. R. Wolbach and H. Zinsser.

Many of the papers were written by men who have worked for a number of years in some phase of the virus field; others represent merely a survey of the literature by a person with no first hand information of the field. All the chapters except the one on distemper have been very well done. One wonders why this was included in the first place, since it is not a human disease and particularly since it is handled in a very perfunctory manner. It would have seemed better to substitute articles on varicella, herpes febrilis and herpes zoster, which, although not as yet definitely

proven to be viral diseases, are generally included in this group.

This book fills a very definite need in bringing our knowledge in this rapidly advancing field up to date and making it easily available. The print is excellent and the charts and illustrations are well presented.

A Handbook of Elementary Psychobiology and Psychiatry. By Edward G. Billings, B.S., M.D., M.D. Cum Laude (Ind.), Assistant Professor of Psychiatry, University of Colorado School of Medicine. 271 pages. New York: The Macmillan Company, 1939. Cloth $2.00.

The practitioner of today is faced with the problem not only of treating disease, but also of orienting a patient who has been overcome by the stress and strain of life in a fast moving world. This compend defines psychology and discusses the basic principles for studying the individual. Methods of psychiatric examination are given and some of the psychopathic states that the physician must contend with are pointed out. This is a book which can give the physician a method of studying the intricacies of the human mind in a minimum of time.

Southern Medical News

LOUISVILLE MEETING

The Southern Medical Association was host to the Jefferson County Medical Society, Louisville, for a dinner meeting at Louisville on Monday evening, May 20, at the Pendennis Club. This meeting was to start off local activities for the Southern Medical Association's annual meeting in Louisville in November. There were two hundred and twenty-five present at this dinner meeting. Dr. E. Lee Heflin, President, Jefferson County Medical Society, spoke briefly in opening the meeting and was followed by Dr. E. L. Henderson, General Chairman for the Louisville meeting, who presented the Chairmen and members of the local committees.

General officers of the Southern Medical Association present were: Dr. A. T. McCormack, Louisville, President; Dr. Quitman U. Newell, St. Louis, President-Elect; Dr. Walter E. Vest, Huntington, West Virginia, Immediate Past President and Member of the Board of Trustees; Dr. Vincent W. Archer, Charlottesville, Virginia, Councilor from Virginia and Chairman of the Council; Dr. Alphonse McMahon, St. Louis, Councilor from Missouri; Dr. Horton Casparis, Nashville, Tennessee, Councilor from Tennessee; Dr. E. W. Rucker, Jr., Birmingham, Alabama, Councilor from Alabama; Dr. E. L. Henderson, Louisville, Councilor from Kentucky; Dr. Irvin Abell, Louisville, a Past President; Mr. C. P. Loranz, Birmingham, Secretary, Treasurer and General Manager; and Mr. Chase Delony, Assistant to Mr. Loranz. For the Southern Medical Association's part of the program addresses were made by Dr. McCormack, Dr. Newell, Dr. Vest, Dr. Archer and Dr. McMahon, Mr. Loranz presiding.

ALABAMA

The Medical Association of the State of Alabama held its annual meeting in Birmingham in April. Dr. S. A. Gordon, Marion, was elected President. The 1941 meeting will be held in Mobile.

Deaths

Dr. Walter S. Rountree, Birmingham, aged 67, died May 6 from a cerebral hemorrhage.

Dr. Noah Franklin Turner, Birmingham, aged 62, was killed February 17 when the automobile in which he was driving was struck by a train.

Dr. Marion Jasper Pruet, Childersburg, aged 71, died March 25 of pneumonia.

Dr. Pinta Prichard, Shawmut, aged 77, died March 1 of carcinoma of the lung.

Dr. Andrew J. Jones, Luverne, aged 82, died April 10.

ARKANSAS

The sixty-fifth annual session of the Arkansas Medical Society was held in Fort Smith the middle of April. The following officers were elected: President, Dr. H. T. Smith, McGehee; President-Elect, Dr. H. Fay H. Jones, Little Rock; First Vice-President, Dr. I. Fulton Jones, Fort Smith; Second Vice-President, Dr. H. V. Kirby, Harrison; Third Vice-President, Dr. C. W. Dixon, Gould; Treasurer, Dr. R. J. Calcote, Little Rock; Secretary, Dr. W. R. Brooksher, Fort Smith, re-elected. The 1941 meeting will be held in Little Rock.

The third series of refresher courses conducted in Arkansas under the auspices of the Committee on Maternal and Child Welfare and the Arkansas State Board of Health will be conducted in a six-week period beginning May 20 by Dr. Jean Valjean Cooke, Associate Professor of Obstetrics at the Washington University School of Medicine, St. Louis. All licensed physicians in Arkansas are invited to the lectures.

The Arkansas State Pediatric Society has elected the following officers for the coming year: President, Dr. C. B. Billingsley, Fort Smith; Vice-President, Dr. W. R. Parsons, Little Rock; Secretary-Treasurer, Dr. Ralph E. Weddington, Fort Smith.

The Arkansas Tuberculosis Association has elected the following officers: President, Dr. A. C. Shipp, Little Rock; Secretary-Treasurer, Dr. S. F. Hoge, Little Rock; Directors: Dr. J. D. Riley, State Sanatorium; Dr. B. E. Barlow, Dermott; and Dr. H. J. Mayfield, El Dorado.

Dr. Earle D. McKelvey, Paragould, has been elected President of the Rotary Club.

Dr. R. M. Sloan, Jonesboro, has been elected Vice-President of the Craighead County Chapter of the National Foundation for Infantile Paralysis.

Dr. Thomas Douglass, Ozark, has been elected President of the Rotary Club.

Dr. J. L. Pickens, Bentonville, has been selected as Assistant Resident Surgeon at Charity Hospital at New Orleans.

Dr. J. O. Leslie, Marshall, has been appointed local surgeon for the M. & A. Railway.

Dr. Charles R. Henry, Little Rock, has resigned as full-time Professor of Obstetrics and Gynecology at the University of Arkansas School of Medicine. He will continue on a part-time basis with the Department.

Dr. H. S. Stern and Miss Jane Rita Ellenbogen, both of Little Rock, were married on March 26.

Deaths

Dr. Edward O. McDermott, Wilmot, aged 74, died February 13 of abscess of the lung following influenza.

Dr. William Delton Jones, Ozan, aged 76, died January 28 of pneumonia.

Dr. Paul T. Vaughan, Hot Springs National Park, aged 69, died March 5 of gastro-enteritis.

Dr. William L. Harper, Junction City, aged 65, died March 22 of carcinoma.

Dr. Edwin Webster Thornton, Piggott, aged 79, died March 1 of arteriosclerosis.

Dr. George Albert Causey, Swifton, aged 66, died March 20.

Dr. Herman Castile, Foreman, aged 51, died March 29 of heart disease.

Dr. Walter H. Estes, Sage, aged 63, died March 29.

Dr. Guy Arnold McCormack, Little Rock, aged 67, died April 6.

Dr. James A. Henley, Marshall, aged 73, died April 14.

DISTRICT OF COLUMBIA

Dr. William Gerry Morgan, Washington, was awarded the highest distinction of the American College of Physicians at its recent meeting in Cleveland when he was made Master of the College, the award being the first one to be made in eleven years.

Former Attorney General Homer S. Cummings has established a special clinic at the George Washington University School of Medicine in memory of the late Mrs. Cummings. The clinic will be supported by the Cecilia Cummings Research Fund and will be devoted to the study of high blood pressure and concomitant ailments. An initial gift of $1,200 a year for a five-year period beginning July 1 has been made available to the University by Mr. Cummings and also provisions for others to contribute. Dr. Paul F. Dickens will be Director of the new clinic.

Dr. Russell J. Fields and Dr. H. Lynn Colvin have been ap-

Continued on page 30

And all I did was clean my screens!

No wonder he's excited! Gone are those unsatisfactory negatives that lacked contrast and detail . . . that often were spotted . . . now that he is using intensifying screens that he keeps clean . . . screens that are free from scratches and nicks. For any dirt or stains on the screens, or imperfections, will make good diagnostic radiography extremely difficult.

Because the use of clean intensifying screens, in good condition, is so important to your radiographs, the Patterson Screen Company has prepared a special booklet entitled "Minutes That Matter". This durably-bound, fully illustrated booklet presents detailed information on screen use and screen care in a new, interesting way. It is designed to be of practical aid in the production of uniformly better negatives.

We will gladly send you a copy of this useful booklet by return mail. Just write for Booklet #194.

THE PATTERSON SCREEN CO
TOWANDA PA., U. S. A.

Patterson
X-RAY
Screens

26 YEARS OF CONCENTRATION ON ONE TASK—THE DEVELOPMENT OF BETTER X-RAY SCREENS

For Patients With Alcoholic Problems

--*The Farm*

A non-institutional arrangement in Howard County, Maryland, for the individual psychological rehabilitation of a limited number of selected voluntary patients with ALCOHOL problems — both male and female — under the psychiatric direction of

Robert V. Seliger, M.D.

CITY OFFICE:

2030 Park Avenue, Baltimore, Md.

Chicago Eye, Ear, Nose & Throat College

Established 1897

231 W. Washington St., Chicago, Ill.

Practical postgraduate course in Ophthalmology and Otolaryngology.

Doctors admitted at any time for review and clinical observation.

OSCAR B. NUGENT, M.D., Director

Continued from page 672

pointed Delegates to the Washington Council of Social Agencies for the ensuing year.

Dr. Henry Beall Gwynn, Washington, and Miss Patricia Hurley, Belmont, Virginia, were married April 12.

DEATHS

Dr. Thomas Allen Groover, Washington, aged 62, died April 10 of carcinoma.

FLORIDA

The Manatee County Medical Society joins the honor roll of 100 per cent paid societies. The officers of the society are: President, Dr. M. M. Harrison; Vice-President, Dr. W. D. Sapp; Secretary-Treasurer, Dr. W. E. Wentzel, all of Bradenton.

The Palm Beach County Medical Society held its last meeting in the form of a dinner, which was presided over by Dr. J. H. Pittman, President of the Society, who introduced Dr. Frank H. Lahey, of Boston, the guest speaker.

Dr. George A. Dame, of Inverness, was host at the last meeting of the Pasco-Hernando-Citrus County Medical Society. Following a scientific meeting in Dr. Dame's office, dinner was served the Society at Jones' Cafe.

The Pinellas County Medical Society is the largest society in the State Association to report 100 per cent paid dues for the year. The officers of the Society are: President, Dr. John A. Herring; President-Elect, Dr. N. W. Gable, Jr.; Vice-Presidents, Dr. M. R. Nickle and Dr. H. D. Solomon; Secretary-Treasurer, Dr. W. C. McConnell, all of St. Petersburg.

The Seminole County Medical Society joins the honor roll of 100 per cent paid societies. The officers of the Society are: President, Dr. Wade H. Garner; Vice-President, Dr. G. S. Bauman; Secretary-Treasurer, Dr. Douglas G. Scott, all of Sanford.

Dr. A. T. Cobb, formerly Physician and Assistant Superintendent of the Florida Farm Colony, has opened offices at Gainesville for the practice of general medicine and surgery.

Dr. Carl S. Lytle, Dunnellon, will locate in Ocala, following the completion of a postgraduate course in surgery at the Cook County Graduate School of Medicine in Chicago.

Dr. Isaac W. Chandler, Avon Park, has recently been appointed a member of the State Board of Medical Examiners.

Dr. Charles Lancaster Clay, Boston, has been appointed Superintendent of the Jackson Memorial Hospital, Miami, to succeed Dr. Robert C. Woodard, who is retiring.

Dr. Carrol T. Bowen, Miami, has been appointed in charge of the Division of Venereal Disease Control of the Duval County Health Unit.

DEATHS

Dr. James H. Montgomery, Gainesville, aged 64, died February 16.

Dr. Mathew W. Spearman, Lake City, aged 58, died March 2 of coronary occlusion.

Dr. George Hanlon Day, Sarasota, aged 61, died March 26 of cerebral hemorrhage.

Dr. John R. Gray, Orlando, aged 80, died March 28.

Continued on page 31

THE JEFFERSON MEDICAL COLLEGE of PHILADELPHIA

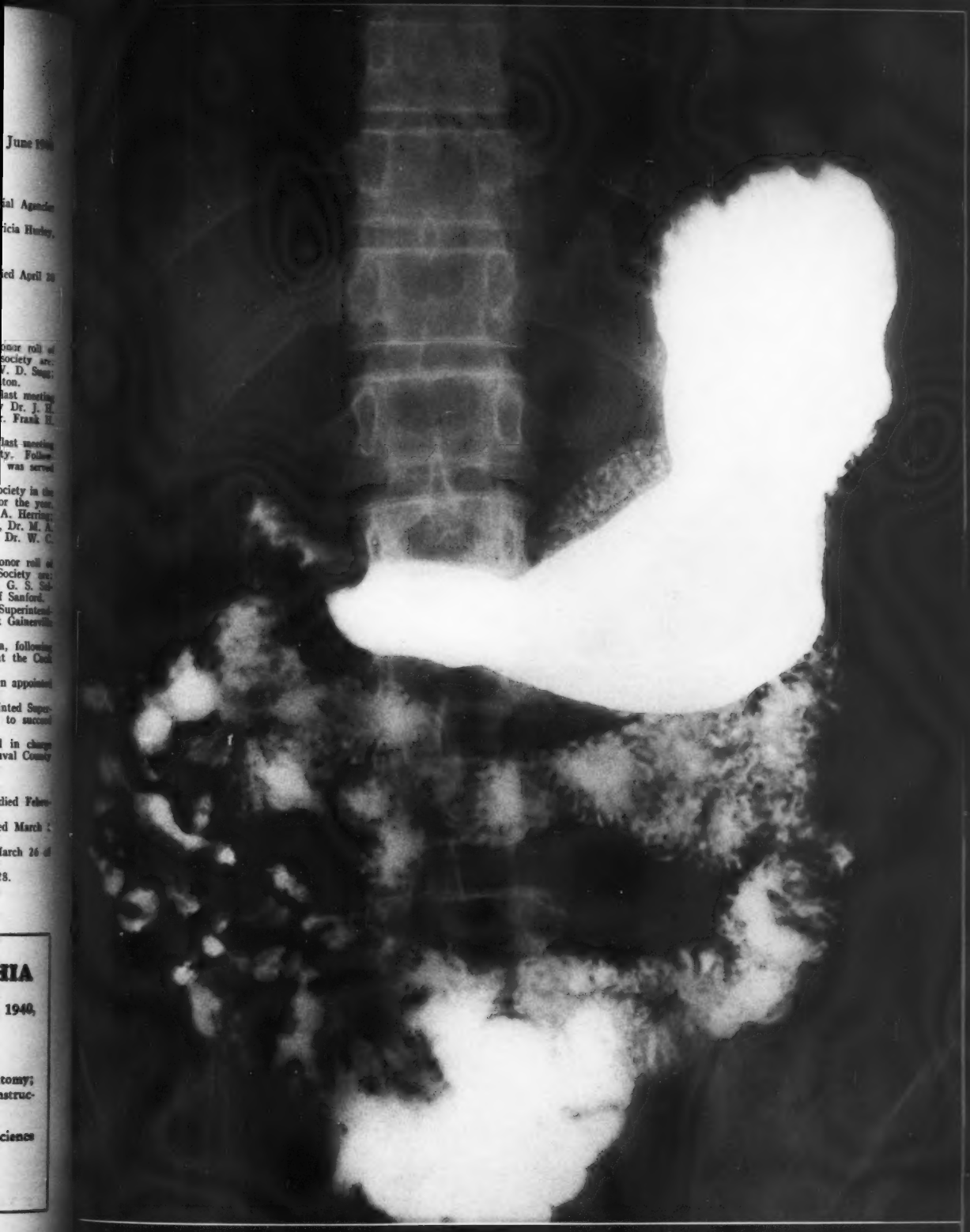
THE ONE HUNDRED AND SIXTEENTH ANNUAL SESSION BEGINS SEPTEMBER 18, 1940, AND ENDS JUNE 6, 1941.

FOUNDED 1825. A chartered university since 1838. Graduates, 16,569.

FACILITIES: Modern, well-equipped laboratories; Curtis Clinic; Daniel Baugh Institute of Anatomy; Department for Diseases of the Chest; Jefferson Hospital; teaching museums and free libraries; instruction privileges in three other hospitals.

ADMISSION: A college degree based on four years of college work including certain specified science and language courses is required.

For full information, address The Dean, The Jefferson Medical College, Philadelphia, Pa.



Reproduced from a radiograph made on

BLUE BRAND EASTMAN ULTRA-SPEED SAFETY X-RAY FILM

(See back of this page)

Excerpt from the Medical Literature....

"Duodenal ulceration is one of the most common affections of the gastro-intestinal tract. The first reports of this condition were described as early as the 16th century, and were based upon autopsy findings. It was not until the development of the roentgen ray that the condition was accurately diagnosed in the living subject.

• • •

"With the advance of the newer radiologic principles in the examination of the duodenal bulb, it is now possible to detect early cases with a high degree of accuracy.

• • •

"A careful radiologic study... aids in demonstrating the early signs of duodenal ulceration and enables the roentgenologist to make an accurate and early diagnosis."

—Am. J. Digest. Dis., *6:* 309, 310, 311, July, 1939

The obvious excellence of the original radiograph reproduced on the reverse side of this page is due, first, to the knowledge of the radiologist; second, to the inherent properties of the new, Blue Brand Eastman *Ultra-Speed* Safety X-ray Film.

»

REFER YOUR PATIENT TO A COMPETENT RADIOLOGIST

«

EASTMAN KODAK COMPANY

Medical Division—Rochester, N. Y.

Be sure to visit the Kodak Building at the New York World's Fair—Kodak in Medicine, Science, Education... a New Cavalcade of Color... photographic experts to assist you. You'll find this a genuinely worth-while exhibit.

(See reverse side of this page)

Continued from page 30

GEORGIA

The memory of Dr. Crawford W. Long, discoverer of ether anesthesia, was honored at a meeting in Jefferson, held in conjunction with the first day sale of the Dr. Crawford W. Long two cent "Famous Americans" postage stamp. The guest of honor was Mrs. Eugenia Long Harper, College Park, aged 85, the only living child of Dr. Long. The Governor, a senator and eminent physicians of the State participated in the program.

Dr. Howard Hailey, President-Elect of the Fulton County Medical Society, and Dr. Hugh Hailey, both of Atlanta, were the recipients of the L. G. Hardman Loving Cup at the meeting of the Medical Association of Georgia in Savannah for their research on "Familial Benign Chronic Pemphigus." L. G. Hardman, physician and late ex-Governor of Georgia, established this award for the most original research work presented by a member of the Medical Association of Georgia in the field of public health, medicine or surgery.

The St. Joseph Infirmary, Atlanta, has elected the following officers: President, Dr. B. McH. Cline; President-Elect, Dr. Major Fowler; Vice-President, Dr. J. G. Riley; Secretary, Dr. Joseph C. Read.

Dr. L. Minor Blackford, Atlanta, has been elected Chairman of the Medical Advisory Committee of the Family Welfare Society and Dr. Joseph C. Massee, Atlanta, has been selected as Vice-Chairman.

Dr. William R. Camp, Fairburn, recently celebrated his fiftieth anniversary in the practice of medicine.

Dr. Robert E. Adair, Cartersville, recently celebrated his fiftieth year in the practice of medicine.

The Blue Ridge Medical Society has elected the following officers for the coming year: President, Dr. J. M. Daves, Blue Ridge; Vice-President, Dr. J. F. O'Daniel, Ellijay; Secretary-Treasurer, Dr. C. B. Crawford, Blue Ridge.

The Stephens County Medical Society has elected the following officers for the coming year: President, Dr. W. B. Heller; Vice-President, Dr. J. E. D. Isbell; Secretary-Treasurer, Dr. C. L. Ayers, all of Toccoa.

The Rockdale County Medical Society has elected the following officers for the coming year: President, Dr. P. J. Brown; Secretary-Treasurer, Dr. H. E. Griggs, both of Conyers.

The Forsythe County Medical Society has elected the following officers for the coming year: President, Dr. Marcus Mashburn; Vice-President, Dr. J. T. Brice; Secretary-Treasurer, Dr. W. E. Lipscomb, all of Cumming.

The Morgan County Medical Society has elected the following officers for the coming year: President, Dr. D. M. Carter; Vice-President, Dr. J. H. Nicholson; Secretary-Treasurer, Dr. W. C. McGeary, all of Madison.

The Ware County Medical Society has elected the following officers for the coming year: President, Dr. Leo Smith; Vice-President, Dr. K. C. Walden; Secretary-Treasurer, Dr. Kenneth McCullough, all of Waycross.

The Chattooga County Medical Society has elected the following officers for the coming year: President, Dr. R. E. Talley; Vice-President, Dr. Mary Margaret McLeod; Secretary-Treasurer, Dr. Lee H. Battle, Jr., all of Trion.

The Ben Hill County Medical Society has elected the following officers for the coming year: President, Dr. Herman Dismuke; Secretary-Treasurer, Dr. J. E. Smith, both of Ocilla.

The Colquitt County Medical Society has elected the following officers for the coming year: President, Dr. James R. Paulk; Vice-President, Dr. Cecil Brannen; Secretary-Treasurer, Dr. R. E. Stegall, all of Moultrie.

The DeKalb County Medical Society has elected the following officers for the coming year: President, Dr. C. E. Cunningham, Decatur; Vice-President, Dr. C. L. Allgood, Scottdale; Secretary-Treasurer, Dr. Lawrence P. Matthews, Decatur.

The Grady County Medical Society has elected the following officers for the coming year: President, Dr. A. B. Reynolds; Secretary-Treasurer, Dr. J. V. Rogers, both of Cairo.

The Lamar County Medical Society has elected the following officers for the coming year: President, Dr. J. H. Jackson; Vice-President, Dr. D. W. Pritchett; Secretary-Treasurer, Dr. S. B. Traylor, all of Barnesville.

The Laurens County Medical Society has elected the following officers for the coming year: President, Dr. J. E. New, Dexter; Vice-President, Dr. D. D. Woodward, Dudley; Secretary-Treasurer, Dr. O. H. Cheek, Dublin.

The Monroe County Medical Society has elected the following officers for the coming year: President, Dr. W. J. Smith, Juliette; Vice-President, Dr. B. L. Smith, Forsyth; Secretary-Treasurer, Dr. G. H. Alexander, Forsyth.

The Polk County Medical Society has elected the following officers for the coming year: President, Dr. Geo. M. White,

Continued on page 32

Harvard Medical School

Courses for Graduates

UROLOGY

By Dr. George Gilbert Smith and Associates at the Massachusetts General Hospital,
July 15-27, inclusive.

This course is designed for physicians who wish to bring their knowledge of urological problems up to date. Fee, $80

ENDOCRINOLOGY and METABOLISM

By Dr. Fuller Albright at the Massachusetts General Hospital,
July 29-August 10, inclusive.

Part I — Parathyroid glands, inorganic salt metabolism, metabolic bone diseases, medical aspect of kidney stone problem, gout, etc.

Part II—Male and female sex hormonology, pituitary diseases, sterility, laboratory tests for pituitary and gonadal hormones, adrenal glands, salt and water metabolism, etc. Fee, $80 for the entire course; $40 for either part.

Apply to Assistant Dean, Courses for Graduates
Harvard Medical School
Boston, Massachusetts

The Tulane University of Louisiana

SCHOOL OF MEDICINE

Review Courses in all branches of medicine annually—January through March.

Special, short time, intensive courses in certain fields may be arranged.

For detailed information write
Director

Department of Graduate Medical Studies
1430 Tulane Avenue, New Orleans, La.

Continued from page 31

Rockmart; Vice-President, Dr. Chas. V. Wood, Cedartown; Secretary-Treasurer, Dr. John M. McGehee, Cedartown.

Dr. James Frederick O'Daniel and Miss Bennetta Lomax, both of Atlanta, were married March 3.

Deaths

Dr. Frank A. Martin, Bowdon, aged 75, died February 27.

Dr. Hugh Nelson Page, Augusta, aged 58, died March 6 of cerebral thrombosis.

Dr. Frank Pattillo Norman, Columbus, aged 54, died on March 17 of heart disease.

Dr. William L. Bennett, Moultrie, aged 68, died March 20 of injuries received in an automobile accident.

Dr. William H. Weeks, Kennesaw, aged 69, died March 15.

Dr. Walter E. Bedingfield, Rentz, aged 60, died March 17.

Dr. Randolph D. Jones, Reidsville, aged 63, died March 29 of heart disease.

Dr. M. N. Wood, Menlo, aged 74, died March 10.

Dr. James Robinson Fuller, Atlanta, aged 57, died March 30.

KENTUCKY

The inaugural Ephraim McDowell Lectureship of the University of Louisville School of Medicine was presented in the amphitheater of the Louisville City Hospital recently with the meeting being opened by Dr. John W. Moore, Dean of the Medical School. Dr. Irvin Abell, an authority on the life of Ephraim McDowell, gave a resume of the life and work of the great Kentucky pioneer surgeon. Dr. M. Herbert Barker, of Northwestern University Medical School, delivered the inaugural lecture entitled "Modern Pioneers in Vascular Diseases." The McDowell lectures are being sponsored annually by the Phi Beta Pi Medical Fraternity.

The Caldwell County Medical Society has elected the following officers for the coming year: President, Dr. I. Z. Barber; Vice-President, Dr. J. M. Moore; Secretary-Treasurer, Dr. W. L. Cash, all of Princeton.

The Graves County Medical Society has elected the following officers for the coming year: President, Dr. W. S. Hargrove, Hickory; Vice-Presidents, Dr. W. E. Merritt, Fancy Farm, and Dr. D. H. Ray, Mayfield; Secretary-Treasurer, Dr. H. H. Hunt, Mayfield. Dr. Hunt has been elected Secretary-Treasurer for life. He has held this office for thirty-six years and is one of the most effective officers of the Association.

The Rockcastle County Medical Society has elected the following officers for the coming year: President, Dr. Walker Owens; Vice-President, Dr. T. A. Griffith; Secretary-Treasurer, Dr. Lee Chesnut, all of Mount Vernon.

Dr. Horace E. Titsworth, Bandana, and Miss Dorothy Goodhue, Chattanooga, Tennessee, were married March 1.

Deaths

Dr. Juanita McFarland Jennings, Louisville, aged 51, died February 24 of carcinoma of the lung.

Dr. Fred Nunn Bybee, Glasgow, aged 38, died March 27 of carcinoma of the rectum.

Dr. Charles Turner Jones, Salt Lick, aged 53, died February 23.

Dr. Reason T. Layman, Elizabethtown, aged 66, died March 27 following an operation for abscess of the gallbladder.

Dr. Oliver Kennett McAdams, Lexington, aged 43, died February 10 of coronary occlusion.

LOUISIANA

Dr. Paul King Rand, Alexandria, was selected as President-Elect of the Louisiana State Medical Society at the recent New Orleans meeting. Shreveport was chosen as the place for the 1941 meeting.

Dr. Oscar W. Bethea, New Orleans, has been appointed Editor of the Yearbook of General Therapeutics.

Dr. Grace Goldsmith, New Orleans, has been elected to Fellowship in the American College of Physicians.

Continued on page 34

Prevent Infection

Outdoor activities at this season cause many minor injuries for which physicians require an antiseptic.

MERCUROCHROME, H. W. & D., satisfies your antiseptic requirements. Tablets or powder provide convenient means of preparing stock solutions. Solutions do not deteriorate, providing for economy in use.

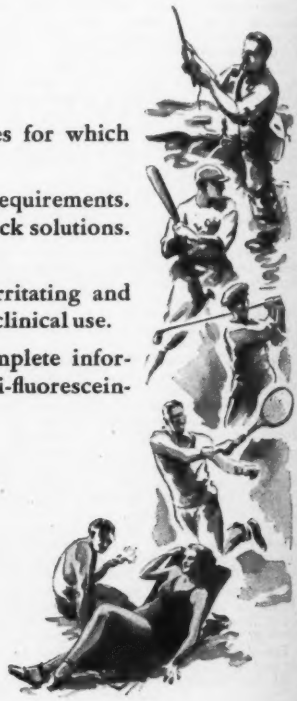
Mercurochrome, 2% aqueous solution, is antiseptic, non-irritating and non-toxic in wounds. It has a background of nineteen years of clinical use.

A comprehensive medical booklet supplying complete information about Mercurochrome (dibrom-oxymercuri-fluorescein-sodium) will be sent to physicians on request.

Mercurochrome. H.W.&D.
(dibrom-oxymercuri-fluorescein-sodium)

ACCEPTED AMERICAN MEDICAL ASSN

Every "H. W. & D." product is investigated and proved chemically, bacteriologically and pharmacologically in our laboratories before marketing.



HYNSON, WESTCOTT & DUNNING, INC.
Baltimore, Maryland

VACOLITER
Infusion
★
Physiological Solution of Sodium Chloride
A Complete Line of Dextrose Concentrations in Normal Saline Solution—2½%, 5%, 7½%, 10%
A Complete Line of Dextrose Concentrations in Distilled Water—2½%, 5%, 7½%, 10%, 20%, 25%
BAXTER TRANSFUSO VAC
Transfusion
★
The Baxter Blood Transfusion Set
★
TRANSFUSO-VACS Containing* 2¼% Sodium Citrate in Normal Saline Solution for 250, 500, 750 cc. of Blood
★
The TRANSFUSO Donor Set
★
Needle Sets 8 and 9 with stainless steel Filterdrip

Maintaining A COMPLETE LINE

A RESPONSIBILITY OF LEADERSHIP

Concentrating in the field of Parenteral Solutions from its first pioneering days, Baxter has made available a range of dextrose and saline solutions which includes *types, percentages, and sizes* to meet every recognized professional requirement.

As new needs are indicated, Baxter promptly meets them with solutions of that chemical and commercial perfection to which its complete facilities have always been devoted.

To hospitals seeking greater efficiency, Baxter offers this wide range of Parenteral Solutions, beyond question as to quality, and available everywhere in a thoroughly satisfactory container — the exclusive VACOLITER with its positive index of vacuum.

Intimately related to Intravenous Infusion is Blood Transfusion, that new phase of Parenteral Therapy in which so many great advances are now being witnessed.

In this field, Baxter pioneered with the original Baxter Blood Transfusion Set; and has continued to pioneer by developing the present widely accepted blood transfusion technique, utilizing the Baxter TRANSFUSO-VAC.

With the Baxter TRANSFUSO-VAC and clot-proof Filterdrip, one operator can perform the entire sequence — Drawing, Citrating, Transporting, Storing, Filtering and Infusing — with continuous aseptic technique. Professional bulletins on request.

ONE OF A SERIES ON THE PROGRESS OF INTRAVENOUS INFUSION AND BLOOD TRANSFUSION.

BAXTER LABORATORIES

Glenview, Ill., College Point, N. Y., Glendale, Cal., Toronto, Canada, London, England

Produced and distributed on the Pacific Coast by Don Baxter, Inc.: Glendale, Cal.

*2¼% Sodium Citrate in Physiological Solution of Sodium Chloride in the Baxter TRANSFUSO-VAC Container.

Distributed East of the Rockies by

CHICAGO • AMERICAN • NEW YORK

HOSPITAL SUPPLY CORPORATION

Continued from page 32

Dr. Richard S. Crichlow, New Orleans, was recently promoted from the rank of Major to Lieutenant Colonel in the Army Reserve Corps.

Dr. Cosmo J. Tardo, New Orleans, was installed recently as President of the Virgilian Society of New Orleans to succeed Dr. E. A. Bertucci.

Dr. Maurice Campagna, New Orleans, was recently appointed Medical Director of the Orleans Tuberculosis Hospital.

Dr. Roy B. Harrison, New Orleans, was elected President of the Missouri Pacific Hospital Association, which recently met in New Orleans.

The Southern Baptist Hospital Staff held its annual banquet at Kolb's Restaurant recently, at which time the following officers were installed: President, Dr. Charles L. Cox; Vice-President, Dr. John T. O'Ferrall; Secretary, Dr. E. Garland Walls; Treasurer, Dr. Robert F. Sharp, all of New Orleans.

The Concordia-Catahoula Bi-Parish Medical Society has elected the following officers for the coming year: President, Dr. N. L. Sebastian, Ferriday; Vice-President, Dr. E. M. Campbell, Ferriday; Secretary-Treasurer, Dr. John Schreiber, Vidalia.

The Louisiana State University School of Medicine announces the formation of an undergraduate honor society under the sponsorship of a faculty committee consisting of Dr. B. I. Burns, Dean; Dr. Charles Midlo and Dr. J. D. Rives. The fourth year membership is limited to the upper tenth of the senior class, and the third year membership to the three highest ranking students in the junior class. The organization is known as The Circle.

DEATHS

Dr. John William Craig, Many, aged 80, died February 12.

Dr. Charles A. Goudchaux, Big Cane, aged 69, died January 27 of acute dilatation of the heart.

Dr. Paul Andrew Lawrence, Mooringsport, aged 68, died in February.

Dr. George R. De Laureal, Broussard, aged 70, died March 4 of cerebral hemorrhage and coronary thrombosis.

Dr. William P. Washington, Rayville, aged 81, died February 28 of chronic myocarditis.

Dr. Timothy A. Duggan, New Orleans, aged 76, died March 6 of carcinoma of the pancreas.

Dr. Oliver C. Teagle, Campti, aged 71, died March 9 of pneumonia.

Dr. James Byron Vaughan, Monroe, aged 63, died April 14.

MARYLAND

Dr. Maynard P. Smith and Miss Mary Helen Young, both of Baltimore, were married January 19.

DEATHS

Dr. Henry Francis Cassidy, Baltimore, aged 70, died February 12.

Dr. George Conkle Shannon, Baltimore, aged 75, died February 13 of pneumonia.

Dr. Alexius McGlannan, Baltimore, aged 67, died February 25 of cerebral hemorrhage, arteriosclerosis, hypertension and auricular fibrillation.

Dr. Emmett Lee Jones, Cumberland, aged 74, died March 31 of mitral regurgitation.

Dr. Roland Ringwalt Diller, Detour, aged 57, died March 10 of myocarditis.

MISSISSIPPI

Dr. W. H. Anderson, Booneville, succeeded to the Presidency of the Mississippi State Medical Association at its closing session in Jackson in May. Dr. Augustus Street, Vicksburg, was elected President-Elect. The retiring President was Dr. J. P. Wall, Jackson. Biloxi will be the meeting place next year.

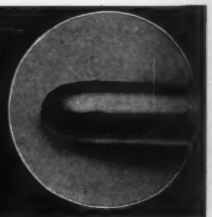
DEATHS

Dr. William Wallace Allred, Collins, aged 58, died March 4 of coronary occlusion, periostitis and cirrhosis of the liver.

Dr. Thomas White Peden, Van Vleet, aged 67, died February 22 of coronary thrombosis.

Continued on page 36

RADON SEEDS



FOR safety and reliability use composite Radon seeds in your cases requiring interstitial radiation. The Composite Radon Seed is the only type of metal Radon Seed having smooth, round, non-cutting ends. In this type of seed, illustrated here highly magnified, Radon is under gas-tight, leak-proof seal. Composite Platinum (or Gold) Radon Seeds and loading-slot instruments for their implantation are available to you exclusively through us. Inquire and order by mail, or preferably by telegraph, reversing charges.

THE RADIUM EMANATION CORPORATION
GRAYBAR BLDG. Telephone MO 4-6455 NEW YORK, N. Y.

FOR THE APPROACHING MALARIA SEASON

chemotherapy

The value of Atabrine, antimalarial chemotherapeutic agent, has been so well established that many physicians look forward to the coming malaria season with assurance that they will be able to cope successfully with this frequently stubborn infection.

In patients treated with Atabrine the parasites disappear from the blood in a relatively short period of time—generally in from two to three days. This is true in tertian and quartan types and applies also to the estivo-autumnal form.

Permanent recovery after Atabrine medication has been observed in a multitude of cases, especially in the southern United States, where low relapse rates have been observed repeatedly. Moreover, the curative effect is generally obtained with a total dosage of only 22½ grains.

ATABRINE

Reg. U. S. Pat. Off. & Canada

Brand of CHINACRIN

Methoxychlordiethylaminopentylamino-acridine

Never advertised to the public!

Visit **WINTHROP'S**
ANESTHESIA EXHIBIT
Medicine and Public Health Building

NEW YORK WORLD'S FAIR 1940

Write for illustrated booklet on malaria and its treatment with Atabrine which includes discussion of dosage and possible side effects.

Winthrop
CHEMICAL COMPANY, INC.
Pharmaceuticals of merit for the physician
NEW YORK, N. Y. WINDSOR, ONT.

723M

Continued from page 34

Dr. Alexander Valentine Hunter, Crystal Springs, aged 72, died March 24 of carcinoma of the pancreas.

Dr. N. D. Guerry, Columbus, aged 75, died April 16.

MISSOURI

Dr. A. R. McComas, Sturgeon, was honored with a testimonial picnic by the Boone County Medical Society on the occasion of his fiftieth anniversary in the practice of medicine, the event being held at the Pinnacles, twelve miles north of Columbia, on Wednesday afternoon, May 22. Dr. Frank G. Nifong, Columbia, presided at the testimonial exercises. Dr. M. Pinson Neal, Columbia, was in charge of the picnic feature. Some two hundred physicians from Boone County and all over Missouri were present to pay honor to their friend and confrere, Dr. McComas.

Dr. Quitman U. Newell, St. Louis, President-Elect of the Southern Medical Association, was a guest of the Mid-South Post Graduate Medical Assembly at Memphis in February, speaking on "The Treatment of Retrodisplacement and Prolapse of the Uterus." On March 11, Dr. Newell spoke to the Medical Department of the University of Alabama at Tuscaloosa on "Sterility in the Female." He addressed the Southeastern Surgical Congress at Birmingham on "Lesions of the Vulva and Their Treatment" on March 12, and on February 26 and 27 he spoke before the New Orleans Graduate Medical Assembly on "Irradiation Therapy in Gynecology" and "Retrodisplacement of the Uterus."

Dr. Llewellyn Sale, St. Louis, President of the St. Louis Social Planning Council, has been made a member of the Committee to present a certificate and prize of $1,000 this Fall to the St. Louisan who they select as having rendered the most outstanding service to the city for the year ending in June.

The Cooper County Medical Society has elected the following officers for the coming year: President, Dr. G. L. Chamberlain, New Franklin; Vice-President, Dr. C. H. Van Ravenswaay, Boonville; Secretary, Dr. J. C. Tincher, Boonville.

The Newton County Medical Society has elected the following officers for the coming year: President, Dr. M. C. Bowman, Neosho; Vice-President, Dr. L. E. Rolens, Granby; Secretary-Treasurer, Dr. John A. Guthrie, Neosho.

The St. Francois-Iron-Madison-Washington-Reynolds County Medical Society has elected the following officers for the coming year: President, Dr. P. L. Jones, Flat River; Vice-President, Dr. W. H. Barron, Fredericktown; Secretary-Treasurer, Dr. G. Tivis Graves, Jr., Farmington, re-elected.

Dr. Duff S. Allen, St. Louis, Assistant Professor of Clinical Surgery, Washington University School of Medicine, delivered the third annual lecture of the University of Arkansas School of Medicine, Little Rock, sponsored by the local chapter of Phi Beta Pi Medical Fraternity on "The Effect of Toxic Goiter on the Heart."

DEATHS

Dr. Thomas Joseph Toner, Wentzville, aged 64, died February 22 of aneurysm of the aorta.

Dr. Louis Edward Printy, St. Louis, aged 51, died February 18.

Dr. Louis William Scherman, St. Louis, aged 61, died February 20 of coronary thrombosis.

Dr. Homer P. Yeater, Cole Camp, aged 71, died February 1 of hypertrophy of the prostate.

Dr. Luther H. Burnett, Kansas City, aged 84, died February 22.

Dr. John B. Atchley, Lebanon, aged 85, died February 25.

Dr. George W. Lott, Westboro, aged 81, died February 10 of coronary thrombosis.

Dr. Robert Greiderer, St. Louis, aged 53, died March 6 of hypostatic pneumonia.

Dr. Daniel E. Cullers, Stella, aged 71, died January 31 of angina pectoris.

Dr. Frank Evans Chase, St. Louis, aged 73, died March 7 of carcinoma.

Dr. Morris Popper, St. Louis, aged 71, died March 10 of heart disease.

Dr. Heine Marks, St. Louis, aged 80, died March 15 of influenza and chronic myocarditis.

NORTH CAROLINA

The portraits of Dr. Jacob Franklin Highsmith and Dr. John DaCosta Highsmith were unveiled in the Rotunda of the Highsmith Hospital in Fayetteville on May 4. Dr. J. F. Highsmith died in June and his son, Dr. J. D. Highsmith, in October of 1939. The elder Highsmith had ministered to his community as

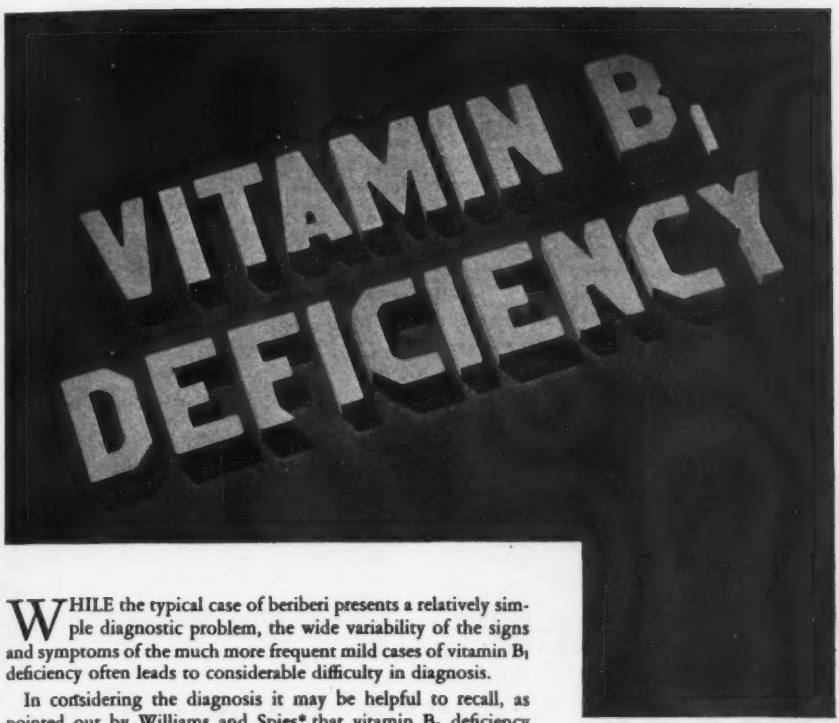
Continued on page 38

for 27 YEARS this Trade-Mark has been YOUR GUARANTEE of
SERVICE
QUALITY
DEPENDABILITY
FINANCIAL RESPONSIBILITY

Manufacturers of
• Puritan MASK AND BAG
• Puritan OXYAERATOR
• Puritan REGULATORS
• Puritan INHALATION UNITS
Write for literature containing complete information
PURITAN COMPRESSED GAS CORP.
GENERAL OFFICES
KANSAS CITY, MISSOURI

Manufacturers of PURITAN MAID Nitrous Oxid : Cyclopropane : Ethylene : Oxygen Carbon Dioxid : Helium : Mixtures of Carbon Dioxid-Oxygen and Helium-Oxygen. Distributors of leading makes of Anesthetic Gas Machines, Oxygen Tents, Resuscitators, Inhalators, Soda Lime, etc.

BRANCHES AND DISTRIBUTING DEALERS IN MOST PRINCIPAL CITIES



WHILE the typical case of beriberi presents a relatively simple diagnostic problem, the wide variability of the signs and symptoms of the much more frequent mild cases of vitamin B_1 deficiency often leads to considerable difficulty in diagnosis.

In considering the diagnosis it may be helpful to recall, as pointed out by Williams and Spies,* that vitamin B_1 deficiency occurs especially among the following groups:

The indigent, and those with improper dietary habits and idiosyncrasies. Poorly balanced diets may be chosen inadvertently or because of financial restrictions. In addition, food fads and reducing diets may be responsible for the development of vitamin B_1 deficiency.

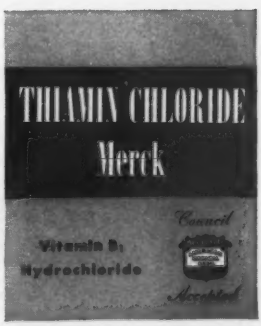
Patients who have an organic disease. In such patients, there may be loss of appetite or restriction of the dietary associated with the disease. In the presence of gastro-intestinal disturbances, the absorption of the vitamin may be impaired.

Persons with increased vitamin B_1 requirements. The requirement for vitamin B_1 is increased as a result of greatly augmented metabolism in febrile conditions, hyperthyroidism, or vigorous muscular exertion, and during pregnancy and lactation.

In cases of vitamin B_1 deficiency, the daily administration of adequate amounts of thiamin chloride will ensure a prompt therapeutic response. When absorption from the gastro-intestinal tract is impaired, parenteral administration of thiamin chloride is indicated.

Literature on Request

*Williams, R. R., and Spies, T. D., Vitamin B_1 and its use in medicine, The Macmillan Co., New York, 1938.



MERCK & CO. Inc. *Manufacturing Chemists* RAHWAY, N. J.

Continued from page 36

physician for fifty years and his hospital was said to be the first private hospital in the State of North Carolina.

Dr. Charles S. Hertz recently joined the staff of the Davis Hospital, Statesville. Dr. Hertz is a graduate of Princeton and the University of Pennsylvania Medical School and has served on the staff of Mayo Clinic for the past four years.

Dr. Adam Thorp, Rocky Mount, has been elected President of the Rotary Club.

Dr. R. H. Lafferty and Dr. O. D. Baxter, Charlotte, announce the association of Dr. P. B. Parsons in the practice of radiology.

The following new appointments to the faculty of the Division of Public Health at the University of North Carolina School of Medicine have just been announced by Dr. Milton J. Rosenau, Director: Dr. John Wright, Research Professor of Epidemiology; Dr. William P. Richardson, Director of Orange, Person and Chatham District Health Department; Dr. Sterling Brackett, Instructor in Public Health.

The Eighth District Medical Society has elected the following officers for the coming year: President, Dr. James McG. McAnally; Vice-President, Dr. P. W. Fetzer; Secretary-Treasurer, Dr. B. F. Cozart, all of Reidsville.

The Ninth District Medical Society has elected the following officers for the coming year: President, Dr. W. H. Kibler, Morganton; Vice-President, Dr. W. D. McLelland, Mooresville; Secretary-Treasurer, Dr. J. Sam Holbrook, Statesville.

The North Carolina Tuberculosis Association has elected the following officers for the coming year: President, Mrs. Charles E. Platt, Charlotte; First Vice-President, Dr. C. W. Armstrong, Salisbury; Second Vice-President, Dr. William H. Smith, Goldsboro; Managing Director, Mr. Frank W. Webster, Winston-Salem, re-elected.

Dr. Addison Brenizer, Charlotte, was named President-Elect of the Tri-State Medical Society at its meeting in Richmond recently.

Dr. Rowland T. Bellows, formerly associated with the University of Rochester Medical School and the Strong Memorial Hospital in Rochester, is now located in Charlotte for the practice of neurosurgery.

Dr. T. R. Huffines, of Asheville, announces the association of Dr. C. C. Belcher, formerly of Alabama.

Dr. J. P. Sullivan, formerly of Massachusetts, is now on the staff of Highlands Hospital in Asheville.

The Duke University School of Medicine at Durham recently had Dr. Edward A. Schuman, Professor of Obstetrics, University of Pennsylvania School of Medicine, to lecture on "Puerperal Infection" and Dr. Thomas Addis, Professor of Medicine, Stanford University School of Medicine, who lectured on "The Treatment of Glomerular Nephritis."

Dr. Ralph Moschella and Miss Helen Homesley, both of Statesville, were married on April 8.

Dr. James Colgate Rudd and Miss Flora Mae Johnston, both of Greensboro, were married on April 16.

DEATHS

Dr. Parrott R. Hardee, Durham, aged 79, died April 14.

Classified Advertisements

RATES for insertion in the Classified Column are as follows: $2.00 minimum, which includes the first 50 words; for each word in addition to the original 50 words, the charge is 3c.

OPENING FOR THREE MIXED RESIDENCIES JULY FIRST. Excellent service. Good salary. Opportunity for one to be chief resident. Address: Superintendent, Roanoke Hospital, Roanoke, Virginia.

WANTED AT ONCE—Graduate of Southern Class A medical school, single, good habits, pleasing personality (Gentile) for assistant in 70-bed private institution. Prefer man with general internship or special training in nervous and mental disorders, drug and alcoholic addictions. Salary $150.00 and maintenance. Dept. 17, SOUTHERN MEDICAL JOURNAL, Birmingham, Ala.

MODERN WELL EQUIPPED CLINIC-HOSPITAL for sale, reasonable price. Located on U. S. highway, in a good town of 2,500 inhabitants, near large gas field in Oklahoma; failing health main reason for selling. Dept. S-51, SOUTHERN MEDICAL JOURNAL, Birmingham, Alabama.

ASSISTANT WANTED—For general practice in coal field. Must be gentile and licensed in West Virginia. Give full particulars in first letter. Geo. W. Johnson, M.D., McAlpin, W. Va.

ASSISTANCE OFFERED TO MEDICAL WRITERS. Research. Abstracts. Translations (all languages). Papers prepared from author's data. Ten years' experience with leading physicians and appointments on medical journals of highest standing. I employ no assistants; all my work is done personally and is reliable. Florence Annan Carpenter, 2220 20th Street, N.W., Washington, D. C.

OKLAHOMA

By way of carrying out the Pneumonia Control Program of Oklahoma, laboratory service, serums and sulfapyridine have been made available to Tulsa and Oklahoma City through the cooperation of the Tulsa and Oklahoma County Medical Societies, the State Health Department and the Department of Bacteriology of the University of Oklahoma School of Medicine. The facilities have been furnished free to those unable to pay for them.

Dr. G. L. Berry, Blackwell, has been elected President of the Blackwell Rotary Club.

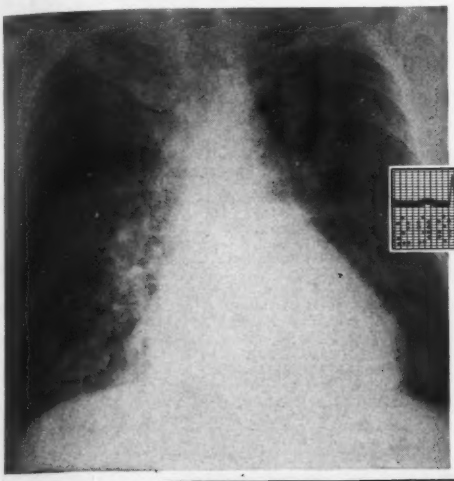
The organization of the Northeastern Oklahoma Medical Association, incorporating county medical societies of the eighth councilor district, was recently effected at a meeting in Muskogee. Representatives from all counties in the district attended the meeting. The new Association is the first one ever organized in that area. Officers are: President, Dr. Wylie G. Chesnut, Miami; Vice-President, Dr. Howell A. Scott, Muskogee; Secre-

Continued on page 40

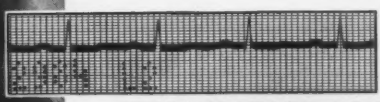
To Assure Quick Dependable Response
Discriminating Physicians are Prescribing
the easily soluble
DUBIN AMINOPHYLLIN
THEOPHYLLINE-ETHYLENEDIAMINE
American Made from American Materials
H.E.DUBIN LABORATORIES
INCORPORATED
250 E. 43rd St. New York, N.Y.

STUDIES IN THE AVITAMINOSES

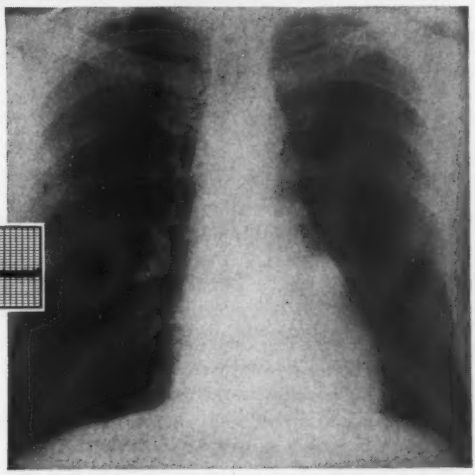
This page is the sixth of a series on vitamin deficiencies presented by the research division of The Upjohn Company because of the profession's widespread interest in the subject. A full color, two-page insert on the same subject appears in the May 25 issue of The Journal of the American Medical Association.



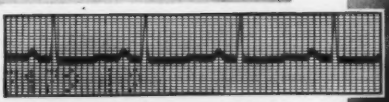
Teleoroentgenogram, at left, of alcoholic patient with severe thiamin deficiency, marked cardiac dilatation, congestive heart failure. X-ray below, taken after three weeks of thiamin chloride therapy, shows marked reduction in cardiac size. Patient received no digitalis.



Electrocardiogram on admission (Lead 2). Note the low voltage of the QRS complexes and of P and T waves. (Left)



After three weeks of thiamin chloride therapy. Note increased voltage, return of P waves. Later tracings showed normal T waves. (Lead 2)



Courtesy of Henry Field, Jr., M.D., University of Michigan.

The Cardiac Manifestations of Vitamin B_1 Deficiency

Vitamin B_1 apparently exerts no specific influence upon the normal heart, but profound deficiency resulting from drastic deprivation may lead to cardiac derangements which are as characteristic as the neural changes at times resulting from thiamin deprivation. In the cases reported, physical examination disclosed that the heart was enlarged to both the right and the left, although on postmortem examination of patients who died of extreme deficiency the enlargement was seen predominantly in the right auricle and ventricle. The former was dilated and paper thin; the wall of the latter appeared thickened and its chamber enlarged. Some difference of opinion exists concerning the mechanism of the increase in cardiac size, since both hypertrophy and edema have been observed by different investigators.

The clinician, through whose courtesy the x-rays and electrocardiograms shown above are made available, states that administration of thiamin chloride promptly led to reduction in the cardiac silhouette.

UPJOHN

Continued from page 38

tary, Dr. W. Jackson Sayles, Miami. The Association, which is purely scientific, will meet three times a year. The next session is scheduled for Miami.

Dr. Raymond E. Mulrooney, recently of Mayo Clinic, Rochester, has joined the staff of the Hardy Sanitarium in Ardmore.

Deaths

Dr. John Washington St. Sing, Kellyville, aged 61, died February 3.

Dr. Darrell Gordon Duncan, Oklahoma City, aged 36, died March 1 of pulmonary tuberculosis.

SOUTH CAROLINA

Dr. George M. Truluck, Orangeburg, was elected President-Elect of the South Carolina State Medical Association at its annual session in Charleston early in May. Dr. W. L. Pressly, Due West, succeeded to the Presidency at that meeting. Dr. Robert E. Seibels, of Columbia, was elected Vice-President and Dr. E. A. Hines, Seneca, re-elected Secretary-Treasurer. The meeting next year will be held at Greenville.

The new building of the Medical College of the State of South Carolina, Charleston, was dedicated with appropriate exercises on Wednesday afternoon, May 1. Addresses were made by the Governor, President of the Alumni Association, President Board of Trustees and others.

Dr. Robert Wilson, Charleston, Dean of the Medical College of the State of South Carolina, was presented with the American Legion's Distinguished Service Plaque on Wednesday afternoon, May 1, during the dedication ceremonies of the new medical school building.

The South Carolina Pediatrics Association has elected the following officers for the coming year: President, Dr. R. B. Josey, Columbia; Vice-President, Dr. George B. Johnson, Spartanburg; Secretary-Treasurer, Dr. George B. Johnson, Spartanburg. Columbia was selected again for the next meeting place.

Dr. L. Emmett Madden, Columbia, was inducted as a Fellow into the American College of Physicans at the last annual meeting in Cleveland.

Dr. R. B. Taft, Charleston, has been elected a member of the Executive Committee of the South Carolina Academy of Science.

The Williamsburg County Medical Association has elected the following officers for the coming year: President, Dr. J. M. Brice, Kingstree; Vice-President, Dr. E. H. Thompson, Kingstree; Secretary-Treasurer, Dr. B. M. Montgomery, St. George.

Dr. R. S. Matthews, Columbia, has resumed his duties as a member of the staff of the South Carolina State Hospital after doing special work in neurology and psychiatry at Harvard University and Boston City and Massachusetts General Hospitals during the past year. Dr. Matthews was honored with a Fellowship by the Rockefeller Foundation.

Dr. George R. Lamb has removed from Columbia, South Carolina, to New Bern, North Carolina.

The South Carolina Urologic Association has elected the following officers for the coming year: President, Dr. R. B. Gantt, Charleston; Vice-President, Dr. S. E. Wheeler, Columbia; Secretary-Treasurer, Dr. Keitt Smith, Greenville, re-elected.

Dr. William L. Perry, Chesterfield, and Miss Ruth Kirven, Darlington, were married on March 23.

Deaths

Dr. Marion Nathaniel Wood, Florence, aged 74, died February 25 of hypertension and cerebral hemorrhage.

TENNESSEE

At the recent annual meeting of the Tennessee State Medical Association the following officers were elected: President, Dr. Leonard W. Edwards, Nashville; Vice-Presidents, Dr. Jesse Paul Baird, Dyersburg, Dr. Joe B. Wright, Lynnville, and Dr. Abraham J. Guinn, Ducktown; Secretary, Dr. Harrison H. Shoulders, Nashville, re-elected.

Dr. R. H. Elder has moved from Sparta to Cedor Hill.

Dr. Jos. C. Wood has moved from Crossville to Tygert Valley Homesteads, Elkins, West Virginia.

Dr. W. B. Harrison has moved from Union City to Hall County Health Unit, Gainesville, Georgia.

Continued on page 42

How much nourishment in a decimal point?

IT ISN'T HARD to reproduce to several decimal points a cow's milk modification that resembles breast milk in *composition*.

But . . . for true *nutritional* resemblance, compensation must be made for the *biological* differences between cow's milk and breast milk.

And the major differences *are* compensated for in Dryco modifications. For one thing, protein content is high because of the biological difference between the protein of cow's milk and the protein of breast milk.

So Dryco modifications provide ample protein throughout the nursing period. And—*just as in breast milk*—Dryco feedings supply highest protein values during early months when growth is fastest and protein need accordingly greatest.

For more than 20 years, Dryco has been clinically proved successful in infant feeding.

DRYCO

A PRODUCT OF THE BORDEN COMPANY

Here's real news! If you have delayed investing in x-ray apparatus until you could be sure that, without exceeding your budget, you could get what you'd really like to have—investigate the new G-E Model R-38 100 milliampere Combination X-Ray Unit.

You want high quality, reliable equipment, of course, and, like all value-wise medical men, you want a unit that will represent a sound, economical investment. The R-38 is just such a unit, and you'll want to check its every feature.

A practical and efficient single-tube unit, the R-38 provides ample power for a wide range of service including fractional-second chest films at six feet. Its double-focus shockproof tube provides fine detail for both radiography and fluoroscopy. Its refined precision control incorporates features that make standardized procedures easy-to-do and duplicate.

The moderately-priced R-38 is an outstanding value. And you owe it to yourself to find out how much more value you will get for your x-ray dollars when you invest in this modern combination unit. Use the convenient coupon to request complete details.

GENERAL ELECTRIC X-RAY CORPORATION A36
2012 JACKSON BLVD. CHICAGO, ILL., U. S. A.

Please send complete information about the NEW G-E Model R-38 Combination X-Ray Unit to

Name.....

Address.....

City.....

State.....

Continued from page 40

Dr. Thomas Wells has moved from Hutchinson to Veterans' Hospital, Alexandria, Louisiana.

Dr. J. D. Henderson, Knoxville, has moved to Alliance, Ohio.

Dr. G. W. Thomasson, Jr., has moved from Nashville to Dallas, Texas.

Dr. Charles M. King has moved from Jackson to Natchitoches, Louisiana.

Deaths

Dr. Ernest A. Downey, Huntland, aged 56, died February 18.

Dr. Caleb C. Cochran, Nashville, aged 90, died February 26 of senility.

Dr. John J. Sledge, Burns, aged 78, died February 29.

Dr. James Benajah Phillips, Chattanooga, aged 58, died March 7 of injuries received in an automobile accident.

Dr. Robert E. Goodlet, Dyersburg, aged 89, died March 10 of a fractured hip

Dr. Tennant Bledsoe Brown, Columbia, aged 66, died March 4 of pneumonia.

Dr. Wesley Wilson Tucker, Lafayette, aged 78, died February 28 of uremia.

Dr. Robert Spicer McDavid, Memphis, aged 47, died March 25 of malignant hypertension.

Dr. Sidney Edward Pincus, Memphis, aged 69, died March 27 of myocarditis.

Dr. Luther H. Montgomery, Trenton, aged 62, died March 16 of coronary occlusion.

Dr. R. E. Fort, Nashville, aged 68, died March 22.

TEXAS

The Delta County Medical Society has elected the following officers for the coming year: President, Dr. Osler Y. Janes; Vice-President, Dr. D. O. Lowry; Secretary-Treasurer, Dr. C. C. Taylor, re-elected, all of Cooper.

The Kerr-Kendall-Gillespie-Bandera Counties Medical Society has elected the following officers for the coming year: President, Dr. Lester Keyser, Fredericksburg; Vice-President, Dr. Elmer Wiedemann, Junction; Secretary, Dr. J. Jackson, Kerrville.

The following physicians: Dr. Leonardo Allen; Dr. Joseph Allen Kyles; Dr. John Mark O'Ferrell; Dr. John T. Moore; Dr. Seeley T. Pulliam; Dr. Martin J. Taylor; and Dr. Elva A. Wright, were recently honored at a dinner marking their retirement after twenty years' active service on the clinics of the charity hospital. They are all of Houston.

A City Hospital for the care of indigent patients was recently opened in Waco under the auspices of the city and the McLennan County Medical Society. The medical society will staff the new hospital, taking turns in the clinics and on the ten medical services.

The Dallas Southern Clinical Society has elected the following officers for the coming year: President, Dr. Everett C. Fox; Vice-President, Dr. Howard Crutcher; Secretary, Dr. Charles H. Warren; Treasurer, Dr. Tom H. Cheavens, all of Dallas.

The All Saints Hospital Staff, Fort Worth, recently elected the following officers for the coming year: President, Dr. W. B. West; First Vice-President, Dr. John W. Garnett; Second Vice-President, Dr. Preston Nesbitt; Secretary, Dr. E. E. Anthony, re-elected.

Dr. P. W. Maline, Big Springs, was recently re-elected President of the West Texas Memorial Association.

Dr. S. D. Whitten, Greenville, has been appointed Hunt County Health Officer to succeed Dr. L. E. Gee, resigned.

Dr. John W. Spies, Dean of the University of Texas School of Medicine, Galveston, was recently elected into the Royal Society of Tropical Medicine and Hygiene in London, in recognition of work he has done in connection with public health.

The Cass-Marion Counties Medical Society has elected the following officers for the coming year: President, Dr. Felix Peebles, Sr.; Vice-President, Dr. A. J. Woods; Secretary-Treasurer, Dr. Felix Peebles, Jr., all of Jefferson.

Dr. R. Louis Cope has moved from Houston to New Orleans.

Dr. Thomas N. Dyson has moved from Austin to Espanola, New Mexico.

Dr. J. C. Duff has moved from Corpus Christi to Anson.

Dr. W. B. Everett has moved from Sterling City to Cleveland.

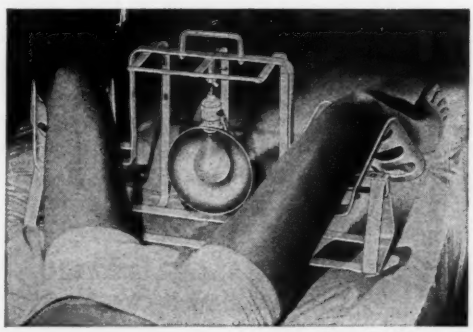
Dr. L. E. Gee has moved from Greenville to Avinger.

Dr. W. F. Perkins has moved from Rusk to Grapevine.

Dr. Guy L. Patillo has moved from Anson to Abilene.

Dr. Frank F. Heger has moved from Tyler to Fort San Houston.

Continued on page 44



THE NEW

Ringo-Westrup

PERINEAL HEATER

SO many makeshifts have been used in perineal heating, without securing proper results, that the Ringo-Westrup Heater has been widely welcomed. Its perfect placement of variable heat to the perineum for relief of pain gives it a place in hospital and office alike. In compact, inexpensive form, it provides easy placement of heat in variable degree, with comfort for the patient and correct application of the thermal benefit. General use is found for the device in post-partum lacerations, after perineorrhaphy, episiotomy, etc. Weighs only ten pounds; has frame holding bed covers off lamp, preventing scorching. Variable heat switch operates by two pull chains. Knee crutches adjust to 3 positions.

PRICE—JP9150—Ringo-Westrup Perineal Heater (uses 40-watt lamp).....$10.75

A. S. ALOE COMPANY

1819 Olive Street **St. Louis, Missouri**

Reducing the Pellagra Death Rate

VEGEX
FOR THE B VITAMIN COMPLEX

In the American Journal of Digestive Diseases, April 1939, page 123, Dr. Frederick R. Taylor of High Point, North Carolina, gives the pellagra death rate of that State for 1923 at 224; for 1928 at 847. The high death rate of 1,015 in 1930 was brought to 327 in 1937. From 1923 to 1928 there was less of organized survey, diagnosis and treatment.

Vegex-Vitafood Dried Brewers' Yeast Aided

With some shipments in 1927, 1928, 1929 and beginning in 1930, there has been upwards of forty thousand pounds of Vegex-Vitafood Dried Brewers' Yeast, Green and Red Label, annually sent into North Carolina; widely distributed from Asheville to Winston-Salem, as well as large amounts into other Southern States.

A questionnaire sent to Southern physicians in 1937 showed that 91.1% of the large number replying use Vegex-Vitafood Dried Brewers' Yeast in successful pellagra treatment; 98% of the forty replying from North Carolina.

This dried brewers' yeast was put into the South at a price to meet the economic level of those afflicted with pellagra; with no other selling except letters to physicians and health departments and, during the last several years, advertisements in the Southern Medical Journal. Further, the best sales survey we can make is that Vegex-Vitafood Dried Brewers' Yeast has been far ahead of any other dried brewers' yeast or dried yeast and the only straight product, without the hop bitterness removed, which has been the main type used in North Carolina and other Southern States.

Current Biological Tests

Current tests show that 20 milligrams—50 International units per gram—give a higher B_1 figure than the reference standard with thiamin and that the Sherman-Bourquin test for B_2 shows 35 plus units per gram. Five per cent in the diet as the sole source of vitamin B complex continues to give good normal growth, reproduction and rearing of the litter with test animals.

Needed with Nicotinic Acid

Within the last several years nicotinic acid has been brought to the aid of pellagra relief, but now with general agreement that it cannot, alone, take the full place of dried brewers' yeast or an extract from it, like Vegex. Needed with the nicotinic acid is either dried brewers' yeast or other sources of the full P-P factor and the full B complex to do the full job.

●

Samples for clinical or professional use will be sent on request

VITAMIN FOOD CO., INC. 122 HUDSON STREET NEW YORK, N. Y. **VEGEX, INC.**

EFFECTIVE THERAPY
IN
Otitis Media
Requires Analgesia
Bacteriostasis, and
Dehydration of the Tissues.
Auralgan
THE DOHO CHEMICAL CORPORATION
New York - Montreal - London

COT-TAR
PIX-LITHANTHRACIS 5%
• Therapeutically active in eczema — particularly suitable in children's eczema.
• Forms a flexible non-peeling coat of tar.
• Can be removed with water or cleansing creams.
• Avoids staining of linen.
• Causes no untoward irritation.
Samples on request
SMJ 6-40
DOAK CO., INC.
CLEVELAND, OHIO

Continued from page 42

Dr. Frank Samuel Griffin, Jr., Liberty, and Miss Helen Shattuck, Alto, were married March 10.

Dr. E. J. Tucker, Liberty, and Miss Lola Dickson were married March 10.

Dr. K. B. Walborn and Miss Annie Evangeline Pool, both of Dallas, were married March 24.

Deaths

Dr. Samuel Carl Red, Houston, aged 78, died February 25.

Dr. Jesse Benton Titterington, Dallas, aged 71, died February 18 of cirrhosis of the liver.

Dr. William Monroe White, Lt. Col. M.C. U. S. Army, Brackettville, aged 61, died January 10 of acute myocarditis.

Dr. David Porter Richardson, Henderson, aged 89, died February 19 of coronary thrombosis.

Dr. John S. Paul, Dallas, aged 62, died March 6 of cerebral hemorrhage and arteriosclerosis.

Dr. Mary King Robbie, San Antonio, aged 60, died March 6 of heart disease and hypertension.

Dr. Joseph Edwin McDonald, Kerrville, aged 46, died March 8 of coronary thrombosis.

Dr. Fred Aswell Turner, Waco, aged 41, died March 29 of acute nephritis and peritonitis.

Dr. Daniel Roberts Brower, Mercedes, aged 65, died March 12 of cerebral arteriosclerosis.

Dr. William S. Fall, Henderson, aged 90, died March 18 of arteriosclerosis.

Dr. C. E. Chandler, Hamilton, aged 54, died March 26 of heart disease.

Dr. J. M. Gober, Beaumont, aged 74, died March 21 of injuries received in an automobile accident.

Dr. Frederick Terrell, San Antonio, aged 84, died March 11.

VIRGINIA

A portrait of the late Dr. James Tate Mason, Seattle, was presented to the University of Virginia Department of Medicine, Charlottesville, recently by friends and members of his class at the University. Dr. Mason, who died in 1936, a few weeks after he was installed in absentia as President of the American Medical Association, graduated from the University of Virginia Department of Medicine in 1905.

The South Piedmont Medical Society has elected the following officers for the coming year: President, Dr. W. L. Eastlack, South Boston; Vice-Presidents, Dr. J. P. Kent, Altavista, Dr. Walter McMann, Danville, and Dr. W. R. Watkins, South Boston; Secretary, Dr. F. O. Plunkett, Lynchburg.

Dr. J. E. K. Flannagan was recently appointed Superintendent and Medical Director of the Municipal Tuberculosis Sanatorium at Roanoke and entered upon his duties there on March 20.

Dr. Alex F. Robertson, Jr., Staunton, recently did postgraduate work at Ann Arbor, Michigan.

Dr. Richard Williamson Fowlkes, Richmond, and Mrs. Ferebee Fenner Cooper, Henderson, North Carolina, were married March 1.

Deaths

Dr. David Lee Hirschler, Norfolk, aged 59, died March 22 of coronary occlusion.

Dr. George Adam Stover, South Boston, aged 67, died April 5.

Dr. Joseph Francis Geisinger, Richmond, aged 57, died April 15.

Dr. Lewis Harvie Taylor, Amelia County, aged 64, died March 30.

Dr. Henry Benjamin Treakle, Richmond, aged 66, died March 30.

WEST VIRGINIA

The Virginia and West Virginia Medical Associations will hold their annual meeting jointly this July 29-31 at White Sulphur Springs, which promises to be a history-making event.

The West Virginia State Medical Association, in conjunction with the State Department of Health, is again offering postgraduate refresher courses for a period of five weeks, starting July 14.

Deaths

Dr. Frederick H. Thaxton, Elkview, aged 59, died February 22 of cerebral hemorrhage.

Dr. Joseph M. Miller, Charles Town, aged 86, died February 28 of senility.

Dr. Comodore Connolly, Vienna, aged 72, died March 16 of coronary occlusion.

Dr. Horace B. Price, Parkersburg, aged 83, died March 24 following pneumonia.

Vitamins alone are not enough!

ADEQUATE MINERAL INTAKE IS OFTEN NECESSARY FOR PROPER VITAMIN UTILIZATION

Recent literature[1] states that calcium deficiency means inability to use vitamin B_1; vitamin A depends upon hemin iron; nicotinic acid should be supplemented by essential minerals; endocrine function requires *both* minerals and vitamins. We have long pioneered the interrelationships of vitamins with minerals through . . .

VI-SYNERAL

VITAMINS **WITH** MINERALS

Vi-Syneral, the original Vitamin-Mineral concentrate, contains the indispensable VITAMINS A,B_1,B_2(G),C,D,E and other B complex factors, fortified with the essential MINERALS: calcium, phosphorus, iron, copper, iodine, manganese, magnesium and zinc in Funk-Dubin balance.

VI-SYNERAL* is taken once daily in palatable capsule or syrup form. Thousands of physicians now prescribe Vi-Syneral as a prophylactic health agent to help maintain maximum fitness of patients during therapy. Only Vi-Syneral offers specially balanced potencies for
(1) Adults, (2) Nursing and Expectant Mothers,
(3) Adolescents, (4) Infants and Children.

*Trade Mark Reg. U.S. Pat. Off.

U. S. VITAMIN CORPORATION
250 EAST 43RD STREET NEW YORK, N. Y.

1. Literature and sample upon request.

He Likes PABLUM

It is a fortunate provision of Nature that at the time the infant is ready to receive the nutritional benefits of cereal, his taste is unspoiled by sweets, pastry, condiments, tobacco, alcohol and other things to which adult palates and constitutions have become conditioned.

Many a parent, with limited knowledge of nutrition, attempts to do the baby's tasting for him. Partial to sweets, the mother sweetens her child's cereal. Disliking cod liver oil, she wrinkles her nose and sighs: "Poor child, to have to take such awful stuff!" The child is quick to learn by example, and soon may become poor indeed—in nutrition, as well as in mental habits and psychological adjustment.

Appreciating the importance and difficulties of the physician's problem in establishing and maintaining good eating habits, Mead Johnson & Company continue to supply Pablum in its natural form. No sugar is added. There is no corresponding dilution of the present protein, mineral and vitamin content of Pablum. Is this not worth while?

Copyright 1939, Mead Johnson & Co., Evansville, Ind., U. S. A.

PABLUM IS NOW SUPPLIED IN TWO NEW SIZES: (1) 1 lb. 2 oz., replacing the 1 lb. size, and offering 2 extra ounces without additional charge; and (2) the new ½ lb. size. This size is small enough to be easily grasped in one hand, is convenient for traveling, and requires only a small outlay of money. Both sizes are more economical in comparison with the former 1 lb. size.

He Likes PABLUM

An Old Pewter Nursing Nipple

of Sainted Memory

but not Sanitary

ATTRACTED by our recent reference to "The Mead Johnson Collection of Ancient Nursing Bottles," a medical friend has sent in as a loan to this interesting historical collection, the pewter nipple shown in the above photograph. The nipple was given to the Doctor some years ago by an old patient who had used it as a child in the 40's. It had also rendered service to her mother, grandmother and other members of her family.

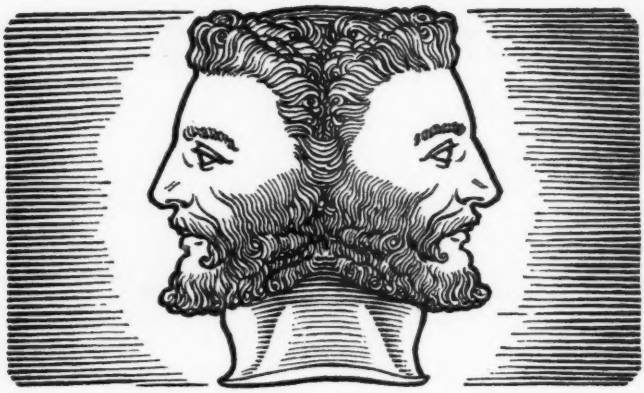
In the eighteenth century, feeding bottles too, were made of pewter, which is an alloy of about 80% tin with copper and lead or antimony. In the wealthier homes, feeding bottles and nipples were made of a special kind of pewter called Britannia metal which contained tin, antimony and copper, sometimes zinc. It was more easily fashioned on the lathe, and could be nickel-plated or silver-plated.

Those were the days before bacteriology, sterilization, etc., and when one examines the long, narrow, inaccessible channel in the pewter nipple (through which the infant sucked his feeding) and sees that this hole could not be kept clean, one realizes how Providence provided for those babies of pre-sanitation days.

Nowadays, babies' bottles and nipples are easily cleansed and sterilized; certified cow's milk contains a permitted maximum of only 10,000 bacteria per c.c. and Dextri-Maltose is practically sterile. Rigid control methods at the dairy and in the Mead Johnson Manufacturing Department, and care in the home combine to give modern babies the sanitary protection not enjoyed by those babies of sainted memory that sucked the pewter nipple illustrated above.

It is significant to reflect that it was through the efforts of physicians that safe, pure milk and sanitary dairy control came to be standardized, and practised, and that Dextri-Maltose came into existence in response to a widespread demand from physicians.

MEAD JOHNSON & CO., EVANSVILLE, IND., U.S.A.



Research must look both ways

Sound research needs Janus-like ability to see in two directions at once—backward for experience—forward for opportunities. Parke, Davis & Company looks *back* on seventy years of research activity—*forward* to new and greater achievement.

The introduction of chemical and physiologic standardization—Adrenalin and Pituitrin—the separation of Pitocin and Pitressin—Mapharsen, Meningococcus Antitoxin—these are a few of the contributions from the Parke-Davis Research Laboratories. Each represents an important chapter in our research experience.

This record must continue; our program points toward tomorrow. Research facilities are constantly being enlarged, activities broadened. Our goal is well defined—to contribute to future medical progress.

PARKE, DAVIS & COMPANY

PIONEERS IN RESEARCH ON MEDICINAL PRODUCTS